From: Collins, Francis (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=410E1CA313F44CED9938E50D2FF0B6C2-COLLINSF]
Sent: 8/14/2020 1:33:23 AM
To: Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257 (b) (6) ; Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770 (b) (6) ; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70- (b) (6)]
CC: Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84 (b) (6)
Subject: RE: Questions about ACTIV EC action items for Friday's teleconference

perfect

From: Wholley, David (FNIH) [T] (b) (6)
Sent: Thursday, August 13, 2020 3:30 PM
To: Collins, Francis (NIH/OD) [E] < (b) (6) Tabak, Lawrence (NIH/OD) [E] < (b) (6)
Parker, Ashley (NIH/OD) [E] < (b) (6)
Cc: Freire, Maria (FNIH) [T] < (b) (6)
Subject: FW: Questions about ACTIV EC action items for Friday's teleconference

Great response! I told Gary I will turn to him to update on these two action items on the call. We will change the responsible party on the first action item from "Preclinical Working Group" to "NIH" and leave the responsible parties on the second as Andy and Gary—I've warned Gary that Andy will not be able to make the call. I think these answers should be sufficient for us to close out these action items after tomorrow. Thanks, David

From: Gibbons, Gary (NIH/NHLBI) [E] (b) (6)
Sent: Thursday, August 13, 2020 1:02 PM
To: Wholley, David (FNIH) [T] (b) (6) >
Subject: Re: Questions about ACTIV EC action items for Friday's teleconference

Hi David,

Thanks for the update/heads up

1. Long term follow-up.
> You are correct, the issue of potential post-infection, long-term effects of COVID-19 has been of interest to NHLBI (and other ICs , particularly NINDS) from the beginning and we have built in a Registry component to our clinical trial "network of networks" platform (we now brand as CONNECTS). This element captures cases that are systematically followed with biospecimen and imaging for long-term followup.

You are correct this effort includes consented individuals who are not enrolled in clinical trials as well as those who are (eg ACTIV4). We are using some of the NHLBI CARES funding that we already received for some of this; but you are correct, the ideal scale up would need additional Congressional supplemental.
— As an alternative approach in addition, we are leveraging NHLBI's legacy longitudinal community-based cohorts (eg Framingham Heart Study; Jackson Heart Study) to capture "community-spread" cases (could be 10% of sample in some areas) and controls and leverage the fact that we already have deep pre-infection characterization (eg imaging), and they are already consented with deep phenotyping protocols for long-term followup.
— This handles case series of 3K-30K.

2. Post-trial Participant Data Tracking.
>> You are correct, the two are thematically related around long-term followup.
— Not much to report as update. Perhaps not a front-burner issue for ACTIV; but helpful to NIH researchers interested in long-term followup surveillance of cases.

Thanks to Andy, we are arranging a meeting between the Reagan-Udall foundation and our team that is establishing the NHLBI's cloud-based data resource platform (BioDataCatalyst) for all NHLBI COVID19 data; and they will dialogue about technology/algorithms (tokenization/hashtags) that would enable us to identify/track clinical trial participants post-trial and follow outcomes by capturing them in EHR databases for long-term followup. We also confirmed that this broader issue of "tokenization"/tracking is also being explored by a trans-NIH COVID WG on Data Resources (ODSS; NLM;NCATS, NHLBI et al)

I hope this clarifies where we stand.

thanks

Best

Gary

From: "Wholley, David (FNIH) [T]" (b) (6)
Date: Wednesday, August 12, 2020 at 10:15:29 PM
To: "Gibbons, Gary (NIH/NHLBI) [E]" (b) (6)
Subject: Questions about ACTIV EC action items for Friday's teleconference

Hi Gary,
We have two action items from previous ACTIV meetings where you were involved in the discussion that are outstanding and that are included on the intro slides to our ACTIV Executive Committee Meeting on Friday:

The Preclinical Working Group was asked to consider treatment of multiorgan residual symptoms in patients who have recovered from moderate and severe disease since this may soon be an urgent area of unmet medical need	**Preclinical Working Group**	**7/29 Leadership Team Meeting**	***In Process – update today***
Gary Gibbons and Andy Plump will follow-up regarding access to natural history studies using available EHR data	Andy Plump, Gary Gibbons	7/15 Executive Committee Meeting; 7/1 Leadership Team Meeting	*In Process – update today*

It seems likely there is a link between these items, and you were certainly involved in both conversations, so I'd like to seek your advice on how to proceed:

1. Action item #1: First of all (and frankly) the attribution of this action item to the ACTIV Preclinical Working Group was probably somewhat arbitrary and misguided. To refresh your memory, the text of the discussion was as follows:

dolstem: 53:23
advances of vaccines, mAbs, a-virals will likely make the window for acute use of immune modulators more narrow. What about the many post-Covid patients w multi-organ residual symptoms? another area to focus on and a translational case for fibroses that can go beyond Covid
Gary Gibbons: 56:49
agreed; reinforces the importance of careful follow-up phenotyping post-trial and natural history studies in recovered patients.
dolstem: 01:10:34
there seems to be so many mAbs going into the clinic, is there possibly a way to prioritize that advances focused solutions faster
walter koroshetz- NINDS: 01:27:49
Michael--The Therapeutics working group was attracted to TXA127, Angiotensin 1-7 peptide, for its promise to reduce pulmonary fibrosis in COVID.
Skip Virgin: 01:30:46
I believe the question of chronic disease for survivors is important. The SARS data on this are potentially very concerning.

I understand from discussions with Francis since then that you and Walter Koroshetz have been recent proponents of a need to mount long term cohort studies of COVID-19 survivors (not just those that are in or will be in an ACTIV trial). Full support of this sounds like it would depend on Congressional approval of supplementary funding, but I understand that NHLBI and NINDS have been at least starting to think about something in this space anyway. I'd like your advice on how you'd like this handled.

2. Seems related to #1, and you have definitely been in the middle of this action item of course, which you asked to keep in the docket for now. Again, question is how you'd like to handle, as I would probably turn to you (and perhaps Andy) for an update to the group on progress towards a solution.

Key for both of these is just to ask what would you be comfortable saying or ask others to say?

Please let me know your perspective when you can.

Thanks, David

From: Collins, Francis (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=410E1CA313F44CED9938E50D2FF0B6C2-COLLINSF]
Sent: 5/11/2020 8:42:49 AM
To: Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]
Subject: RE: passive immunization protocols

Yes, that Gary.

From: Tabak, Lawrence (NIH/OD) [E] < (b) (6)
Sent: Sunday, May 10, 2020 10:34 PM
To: Collins, Francis (NIH/OD) [E] < (b) (6)
Subject: Re: passive immunization protocols

yes, I assuming you mean Gary Disbrow.

From: Francis Collins (b) (6)
Date: Sunday, May 10, 2020 at 10:26 PM
To: "Tabak, Lawrence (NIH/OD) [E]" < (b) (6)
Subject: RE: passive immunization protocols

We have to do something about the current situation, that's for sure.

Shall I set up a call with Gary?

FC

From: Tabak, Lawrence (NIH/OD) [E] (b) (6)
Sent: Sunday, May 10, 2020 10:14 PM
To: Collins, Francis (NIH/OD) [E] (b) (6)
Subject: Re: passive immunization protocols

Should you insist that all proposal for BARDA resources be reviewed (signed off by) you?

From: Francis Collins (b) (6)
Date: Sunday, May 10, 2020 at 10:02 PM
To: "Lane, Cliff (NIH/NIAID) [E]" (b) (6)
Cc: "Tabak, Lawrence (NIH/OD) [E]' (b) (6) "Wholley, David (FNIH) [T]" (b) (6) "Adam, Stacey (FNIH) [T]" < (b) (6) "Parker, Ashley (NIH/OD) [E]" (b) (6)
Subject: passive immunization protocols

Hi Cliff,

In a very recent e-mail with Gary Gibbons about anticoagulation protocols, he provided this additional information:

In addition to host-directed anti-thrombotic interventions, our team and PI community have been engaged with BARDA for over a month to line up studies using hyperimmune globulin from convalescent plasma. We were planning on including this element in the

MPs our networks have been working on pre-ACTIV. We vetted and approved the first element of the "passive immunization" MP in our networks over the past 2 weeks and BARDA has already committed to covering the entire cost.

We (and our PI community) believe that a "passive immunization" approach using blood-derived products offers one of the fastest and most promising treatments to offer COVID patients during this uniquely opportune window prior to availability to vaccines. As the team has begun to learn more about the ACTIV MP; it still appeared that this "passive immunization" intervention approach was ***not*** *evident to us in the MP of ACTT2 or ACTT3. We believe this class of therapeutics should be a high priority for incorporation into an ACTIV MP.*

I was therefore quite intrigued by your comment/annoucment at the Wed meeting regarding the prospects of bringing Takeda's hyperimmune globulin under the ACTIV banner. I look forward to hearing guidance on how this approach may be incorporated into a coherent ACTIV MP.

One possible option for consideration might be for us to include a combination of anticoagulation and passive immunization as core elements of a "ACTT-2B" MP. In a fashion analogous to NIAID's ACTT2 protocol; we might consider a similar approach with a MP that includes Remdesivir as the standard background treatment in support of arms testing these anticoagulation and passive immunity interventions. Although the NIAID and NHLBI teams are engaged in ongoing dialogues, this could be an opportunity for the ACTIV umbrella to create convergence of these efforts and Master protocols.

I confess was not aware that NHLBI was already moving down this path, or that they had already negotiated support from BARDA. I agree that passive immunization is one of the more promising short term therapeutic approaches for COVID-19, and I don't want to do anything to slow that down. But I know that NIAID is also very interested in this area, and have been working with Takeda on IVIG. Were you aware of NHLBI's efforts, and is there a need (perhaps through ACTIV) to bring these together?

Francis

From: Collins, Francis (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=410E1CA313F44CED9938E50D2FF0B6C2-COLLINSF]
Sent: 12/29/2020 9:10:48 PM
To: Menetski, Joseph (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5001af52dc4a427ea3d34f1e072f8cb7-menetskijp]
CC: Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]
Subject: RE: Mutation tracking proposal

Great to have these numbers, let's see what Moncef says about the most recent response I sent this morning.

Francis

From: Menetski, Joseph (FNIH) [T] < (b) (6)
Sent: Tuesday, December 29, 2020 3:14 PM
To: Collins, Francis (NIH/OD) [E] < (b) (6)
Cc: Wholley, David (FNIH) [T] < (b) (6) Freire, Maria (FNIH) [T] < (b) (6) Menetski, Joseph (FNIH) [T] < (b) (6)
Subject: RE: Mutation tracking proposal

Dear Francis,

I have generated 2 modified proposals for 1 year term based on the number of proposed variants tested. The costs are:

- 40 variants $16,350,000
- 50 variants $18,375,000

Let me know if you need the 1 year proposals, but I thought you might want to know that actual costs for each number of variants.

Best regards,
Joe

From: Collins, Francis (NIH/OD) [E] (b) (6)
Sent: Tuesday, December 29, 2020 11:00 AM
To: Slaoui, Moncef (b) (6)
Cc: Menetski, Joseph (FNIH) [T] (b) (6)
Subject: RE: Mutation tracking proposal

Hi Moncef,

Thanks for your quick response. The number I mentioned over the phone was for a scaled-down one-year effort, but it's hard to imagine this being a need that goes away after December 2021. The current proposal is rather more ambitious than what we discussed, designed to cover 120 total variants/year for three years. We think that this volume of mutation research studies is entirely justifiable – but a 40 variant/year proposal (more like what we discussed by phone) would be (b) (5) Years 2 and 3 are based on the efforts from year 1, so would also scale with variants (though there are up front costs that make the first

year moderately more expensive). I can send a revised proposal for the 40 variants/year scale, if that would be helpful.

CDC is a major contributor to the proposal, and there is a (b) (5) in the first year to enhance their sequencing efforts. CDC will need to be the main driver of the emerging surveillance effort and a contributor to testing. This proposal is meant to augment and accelerate the process across USG and include industry involvement.

Let me know what I can to help with this consideration.

Francis

From: Slaoui, Moncef (b) (6)
Sent: Tuesday, December 29, 2020 9:04 AM
To: Collins, Francis (NIH/OD) [E] (b) (6)
Subject: RE: Mutation tracking proposal

Hi Francis
Thank you for following up .
We will look into this of course, but two points I would like to share

1- (b) (5)

2-

Thank you
Moncef

From: Collins, Francis (NIH/OD) [E] (b) (6)
Sent: Tuesday, December 29, 2020 8:08 AM
To: Slaoui, Moncef < (b) (6)
Cc: Menetski, Joseph (FNIH) [T] (b) (6) Anderson, James (NIH/OD) [E] (b) (6) >; Tabak, Lawrence (NIH/OD) [E] (b) (6) >; Wholley, David (FNIH) [T] (b) (6) >; Freire, Maria (FNIH) [T] (b) (6) ; Lane, Cliff (NIH/NIAID) [E] (b) (6) Fauci, Anthony (NIH/NIAID) [E] (b) (6) ; Erbelding, Emily (NIH/NIAID) [E] (b) (6) Marston, Hilary (NIH/NIAID) [E] (b) (6) >; Woodcock, Janet (FDA/CDER) (b) (6) ; Hepburn, Matt (HHS/IOS) (b) (6)
Subject: Mutation tracking proposal

Hi Moncef,

As discussed with you briefly by phone last week, the ACTIV Preclinical Working Group has been hard at work shaping a program that would track newly arising mutations in SARS-CoV-2 and gather information quickly about their significance. Up until now, this has been a bit of a scattershot effort, with a lot of work going on in separate public and private organizations, but no agreement for immediate sharing of the data in a publicly accessible database. The recent emergence of variants in the UK and South Africa has added further urgency to this effort, though this ACTIV plan began before those gained wide public attention.

Attached is a five-step proposal about how to organize a much more effective approach, with significant input from industry, NIH, CDC, and FDA. The three-year budget comes to (b) (5) I would appreciate your thoughts about how best to proceed with this request for support.

I'd be glad to discuss this further by phone if that would be helpful. Joe Menetski of the Foundation for NIH has been the primary curator of the plan, and would also be glad to provide further details about the components of the plan.

Best, Francis

From: Adam, Stacey (FNIH) [T] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=DCD875F0679648859E1CF101C0943414-ADAMSJ4]
Sent: 8/19/2020 1:20:21 PM
To: Woodcock, Janet (FDA/CDER) [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=9bc3fc3ebfcf48879f92169bd7644e29-Janet.Woodc]; Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]
CC: Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Austin, Christopher (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=17597cabc42247548e596778304f781f-austinc]; Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]; Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Fauci, Anthony (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=df38103d75134f658ae2d356f0396b94-afauci]; Lane, Cliff (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]
Subject: RE: ACTIV 2 and 3 trial activation and enrollment

Hi Janet,

Okay, I will invite Rachel and Bill to the TOC for today, and include Vickie Davey from the VA. However, judging from your note below, I will not invite the CRO leads from PPD for ACTIV-2. I will rearrange the schedule to have this discussion upfront and push our agent review to the end. We can likely do that in shortened time if we need to.

Thanks,
Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: (b) (6) | Mobile: (b) (6)

From: Woodcock, Janet < (b) (6)
Sent: Wednesday, August 19, 2020 9:14 AM
To: Wholley, David (FNIH) [T] < (b) (6) Collins, Francis (NIH/OD) [E] < (b) (6)
Cc: Adam, Stacey (FNIH) [T] < (b) (6) Freire, Maria (FNIH) [T] < (b) (6) Austin, Christopher (NIH/NCATS) [E] < (b) (6) Anderson, James (NIH/OD) [E] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6) Tabak, Lawrence (NIH/OD) [E] < (b) (6) Fauci, Anthony (NIH/NIAID) [E] < (b) (6) Lane, Cliff (NIH/NIAID) [E] < (b) (6)
Subject: RE: ACTIV 2 and 3 trial activation and enrollment

Thanks. I'd include our folks, Rachel and Bill, as they have been working to identify these problems. There is an issue with the CRO for ACTIV 2, they have not been as coordinated and aggressive on site activation as we need. This probably needs to be dealt with separately outside of the TOC. We also may need to accelerate the plan for activating the non-academic sites. The military has some sort of contract with a firm with trailer units that can be put into place, we (OWS)

are evaluating that. The remdesivir shortage may have impacted ACTIV 3 a bit, I have been trying to resolve that and it should be improved very soon. But particularly with the OP study we need to talk to the PIs about a sense of urgency. We don't have a year to get these studies done.

I'd use the time to find out from the PIs what they think is going on and to make a plan. jw

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From: Wholley, David (FNIH) [T] (b) (6)
Sent: Wednesday, August 19, 2020 9:00 AM
To: Collins, Francis S (NIH) (b) (6) ; Woodcock, Janet (b) (6)
Cc: Adam, Stacey J (NIH) < (b) (6) ; Freire, Maria C (NIH) < (b) (6) ; Austin, Christopher P (NIH) < (b) (6) ; Anderson, James M (NIH) < (b) (6) ; Parker, Ashley S (NIH) (b) (6) ; Tabak, Lawrence A (NIH) (b) (6) ; Fauci, Anthony S (NIH) < (b) (6) ; Lane, Henry C (NIH) (b) (6) >
Subject: RE: ACTIV 2 and 3 trial activation and enrollment
Importance: High

Hi Francis and Janet:
Stacey and I just discussed this. We actually have the ACTIV 2/3 Trial Oversight Committee at 3PM today. It has most of the high level players with the exception of the VA and the CRO leads. We could try to invite their reps to this if you wish (see if we can get them at this point) and turn the agenda toward these issues since they seem most pressing. We can decide at that meeting whether we then need calls with sites, since that involves getting availability from a bunch more folks. Janet, please let us know what you think will work best and we will swing into action.

David

From: Collins, Francis (NIH/OD) [E] (b) (6) >
Sent: Wednesday, August 19, 2020 8:48 AM
To: Woodcock, Janet (FDA/CDER) (b) (6)
Cc: Adam, Stacey (FNIH) [T] (b) (6) Wholley, David (FNIH) [T] (b) (6) >; Freire, Maria (FNIH) [T] < (b) (6) ; Austin, Christopher (NIH/NCATS) [E] < (b) (6) ; Anderson, James (NIH/OD) [E] (b) (6) ; Parker, Ashley (NIH/OD) [E] (b) (6) ; Tabak, Lawrence (NIH/OD) [E] < (b) (6) ; Fauci, Anthony (NIH/NIAID) [E] (b) (6) ; Lane, Cliff (NIH/NIAID) [E] (b) (6)
Subject: RE: ACTIV 2 and 3 trial activation and enrollment

Hi Janet,

We just discussed the situation with ACTIV-2 and ACTIV-3 at the morning War Room meeting. We all agree that immediate action is needed, and the next step ought to be to gather the appropriate principals (probably including some enrollment site PIs) to identify the obstacles and figure out how to get past them. David Wholley and Stacey Adam are set to organize that conference call in the next day or two. That will need to involve the appropriate Division leadership from NIAID (Peter Kim, Cliff Lane) as well as other partners (maybe the VA? No enrollments there yet for ACTIV-3). David will want to know from you -- should the ACTIV-2 CRO be included? Whom from OWS should be involved besides yourself?

Let's get this figured out and fixed!

Francis

From: Collins, Francis (NIH/OD) [E]
Sent: Tuesday, August 18, 2020 3:47 PM

To: Woodcock, Janet < (b) (6) Tabak, Lawrence (NIH/OD) [E] (b) (6) Fauci, Anthony (NIH/NIAID) [E] (b) (6) >; Lane, Cliff (NIH/NIAID) [E] (b) (6)
Cc: Adam, Stacey (FNIH) [T] (b) (6) >; Wholley, David (FNIH) [T] (b) (6) >, Freire, Maria (FNIH) [T] (b) (6) ; Austin, Christopher (NIH/NCATS) [E] (b) (6) Anderson, James (NIH/OD) [E] (b) (6) >; Parker, Ashley (NIH/OD) [E] (b) (6)
Subject: RE: ACTIV 2 and 3 trial activation and enrollment

Hi Janet,

Thanks for your note. I agree completely that these challenges with recruitment to ACTIV-2 need to be tackled head on. I'm looping in Stacey Adam and the other members of the ACTIV War Room to see what other suggestions they might have. I am happy to call anyone anytime if it would help to convey the sense of urgency and high pr ority.

Francis

From: Woodcock, Janet (b) (6)
Sent: Tuesday, August 18, 2020 12:55 PM
To: Collins, Francis (NIH/OD) [E] < (b) (6) Tabak, Lawrence (NIH/OD) [E] (b) (6) Fauci, Anthony (NIH/NIAID) [E] (b) (6) Lane, Cliff (NIH/NIAID) [E] (b) (6)
Subject: ACTIV 2 and 3 trial activation and enrollment

After heroic efforts by all involved to get these studies up and running, we now face the issue of continuing the momentum. ACTIV 2 has not yet enrolled the first patient. ACTIV 3 has been "going slow" since there was limited safety data on the antibody, but after 27 infusions and no SAEs, they will continue to enroll and have a DSMB look at the safety data on Aug 31. At that point, they should be poised to enroll very quickly. As you know, it is poss ble there will be a convalescent plasma EUA and that could detract from enrollment in this study, as will the HIG RCT being done by INSIGHT. The main bottleneck will be study personnel bandwidth, not patient availability.

Diagnostics have been done on ACTIV 2 and some solutions are being put into place. Site activation is problematic and the CRO needs to step up. The OWS leadership has offered to bring in freestanding trailers that can be used for infusions and visits, since despite Francis's email about the urgency space is still begrudged at some of the sites, and at some it s just not available. Rapid diagnostics have been obtained.

ACTIV 3 has an ambitious plan to bring on more sites in the upcoming weeks. The remdesivir issue is resolving.

Nevertheless the formal projections of milestones for these studies stretch way into the new year. We need evaluation much faster if we are to impact this outbreak.

I propose that the NIH leadership work with OWS (me and others) to develop some realistic but aggressive goals and timelines to negotiate with the study teams. I recognize that everyone is burdened but this needs to be made a priority and any support needed should be surfaced and provided. Please let me know what you collectively think about this.

jw

From: Patterson, Amy (NIH/NHLBI) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=AFAD1CA74B3E449D8B4F3191D658B70F-PATTERSA]
Sent: 3/1/2021 1:22:49 AM
To: Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]
CC: Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Gibbons, Gary (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=b71b953b50a5495ca0f2869ab13bc407-gibbonsgh]; Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Lane, Cliff (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]; Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]; Rutter, Joni (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=157b2517ddb546a8a72844c35eadb062-jrutter]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]
Subject: RE: Termination of C3PO

Less than 7 days, I believe. But will double check.
Amy

From: Collins, Francis (NIH/OD) [E] < (b) (6)
Sent: Sunday, February 28, 2021 8:20 PM
To: Patterson, Amy (NIH/NHLBI) [E] < (b) (6)
Cc: Tabak, Lawrence (NIH/OD) [E] < (b) (6) Gibbons, Gary (NIH/NHLBI) [E] < (b) (6) Tabak, Lawrence (NIH/OD) [E] < (b) (6) Wholley, David (FNIH) [T] < (b) (6) Freire, Maria (FNIH) [T] < (b) (6) Lane, Cliff (NIH/NIAID) [E] < (b) (6) Anderson, James (NIH/OD) [E] < (b) (6) Rutter, Joni (NIH/NCATS) [E] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6)
Subject: RE: Termination of C3PO

Thanks. And what was the range of time intervals from onset of symptoms to infusion?

Francis

From: Patterson, Amy (NIH/NHLBI) [E] (b) (6)
Sent: Sunday, February 28, 2021 8:19 PM
To: Collins, Francis (NIH/OD) [E] < (b) (6)
Cc: Tabak, Lawrence (NIH/OD) [E] < (b) (6) Gibbons, Gary (NIH/NHLBI) [E (b) (6) Tabak, Lawrence (NIH/OD) [E] (b) (6) Wholley, David (FNIH) [T] (b) (6) , Freire, Maria (FNIH) [T] (b) (6) ; Lane, Cliff (NIH/NIAID) [E] (b) (6) Anderson, James (NIH/OD) [E] < (b) (6) Rutter, Joni (NIH/NCATS) [E] < (b) (6) , Parker, Ashley (NIH/OD) [E] < (b) (6)
Subject: RE: Termination of C3PO

Hi Francis,
Important question. The study population included adults presenting to the emergency department with their first episode of symptomatic, laboratory-confirmed COVID-19 illness, who were at high risk for progression to severe/critical illness, but who were clinically stable for outpatient management at randomization. Specific inclusion criteria included one or more symptoms of COVID-19 illness and laboratory-confirmed SARS-CoV-2 infection; at least one study defined risk factor for severe COVID-19 illness; and being deemed by ED team to be stable for outpatient management without new supplemental oxygen requirement. Study defined risk factors initially included. age ≥50 years, hypertension; diabetes; coronary artery disease; chronic lung disease; chronic kidney disease; immunosuppression; sickle cell disease, and obesity (body mass index [BMI]≥30) and were updated as needed (e.g., in response to changes in CDC guidance or other information).
Amy

From: Collins, Francis (NIH/OD) [E] < (b) (6)
Sent: Sunday, February 28, 2021 8:04 PM
To: Patterson, Amy (NIH/NHLBI) [E] <(
Cc: Tabak, Lawrence (NIH/OD) [E] < (b) (6) Gibbons, Gary (NIH/NHLBI) [E] (b) (6) Tabak, Lawrence (NIH/OD) [E] (b) (6) Wholley, David (FNIH) [T] < (b) (6) Freire, Maria (FNIH) [T] (b) (6) >; Lane, Cliff (NIH/NIAID) [E] (b) (6) Anderson, James (NIH/OD) [E] < (b) (6) Rutter, Joni (NIH/NCATS) [E] (b) (6) Parker, Ashley (NIH/OD) [E] (b) (6)
Subject: RE: Termination of C3PO

Wow, that's big news. I'm looping in the ACTIV War Room. Recognizing that the benefit of convalescent plasma would be greatest in high risk individuals, were those significantly represented in the C3PO enrollment?

Francis

From: Patterson, Amy (NIH/NHLBI) [E] < (b) (6)
Sent: Sunday, February 28, 2021 7:14 PM
To: Collins, Francis (NIH/OD) [E] < (b) (6)
Cc: Tabak, Lawrence (NIH/OD) [E] < (b) (6) Gibbons, Gary (NIH/NHLBI) [E] < (b) (6)
Subject: Termination of C3PO

Hi Francis,

We wanted to let you know that the C3PO DSMB met and recommended termination of the trial due to futility – there was no statistical difference in the primary endpoint (death, hospital admission, or seeking emergency or urgent care within 15 days of randomization) between participants receiving convalescent plasma and those receiving placebo. NHLBI, in consultation, with NINDS, has accepted this recommendation and the investigators have been notified so enrollment and treatment would stop immediately. FDA has of course been looped in. Our communications team is working on a press statement and other materials for the public and, as always, will work in concert with OCPL.

The SIREN network will not be idle, however! As previously discussed , SIREN does have some sites with outpatient capacity positioned so that they can contribute to ACTIV-6 and other studies. However, as the network leadership of SIREN has emphasized, they're best suited for trials in the Emergency Department (ED) given the scope of the network and the focus in the emergency medicine space; with this in mind, SIREN plans to pivot now to an adaptive protocol developed for moderate to severely ill patients that present to the ED in an extension of the ACTIV-4 platform to this clinical setting and targeting host-tissue response pathways (e.g., inhibition of thrombo-inflammatory cascade, NETS production, and platelet aggregation). This could include collaboration with some of the other ACTIV studies with co-enrollment as we have done to date. NHLBI and NINDS can discuss these recent events and the plans with the ACTIV group in the next couple of weeks.

We'll keep you posted of any additional developments, and in the meantime, please don't hesitate to reach out if you have any questions or concerns.

Regards,

Amy

From: Collins, Francis (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=410E1CA313F44CED9938E50D2FF0B6C2-COLLINSF]
Sent: 7/31/2020 9:10:51 AM
To: Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Austin, Christopher (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=17597cabc42247548e596778304f781f-austinc]; Lane, Cliff (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]; Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]
Subject: FW: Enrollment and Budgets for CP Trials
Attachments: CP RCT Enrollment and Costs Chart 073020 5PM.pptx

For discussion

From: Collins, Francis (NIH/OD) [E]
Sent: Thursday, July 30, 2020 9:16 PM
To: Parker, Ashley (NIH/OD) [E] < (b) (6)
Cc: Kurilla, Michael (NIH/NCATS) [E] < (b) (6)
Subject: RE: Enrollment and Budgets for CP Trials

Hi Ashley,

Thanks for putting this all together. I'm not quite sure in some instances whether the budget figures attach to August 31 or September 30.

The JHU Outpatient trial is extremely expensive -- $260K/patient, more than ten times all of the others except Vanderbilt, which is also quite high at $53K/patient. The others are $1.4K/pt (C3PO, wonder if they left something out) or $10K-17K/pt (NYU group).

I'm inclined to say let's pull out all the stops for Sept. 30 on C3PO (600, but will need help with testing), Miami (360) , and Houston (with AL/MS, 400). NYU/Einstein will need some support for supply of CP and doing titers. Estimated total about 1360 patients, for $10.5M. Vanderbilt says they could provide another 600, but the price is way too high (too much overhead for all these centers?), they'd have to come way down.

Mike, does that look right to you?

Let's discuss at War Room tomorrow.

Francis

From: Parker, Ashley (NIH/OD) [E] (b) (6) >
Sent: Thursday, July 30, 2020 6:07 PM

To: Collins, Francis (NIH/OD) [E] (b) (6)
Cc: Kurilla, Michael (NIH/NCATS) [E] (b) (6)
Subject: Enrollment and Budgets for CP Trials

Hi Francis,

Attached is the most recent version of the enrollment and budget numbers for the CP trials. I spoke with Mike Kurilla, cc'd here to confirm the budgets for the NCATS supported trials given we received quite a few changes today for UT Houston and UMiami. Also included are the common barriers to accrual and recommendations to accelerate enrollment.

Totals:

- JHU—$40-50M (Dan to send detailed breakdown on Monday)
- SIREN/C3PO—$1M
- NYU—$2M
- UMiami—$5.5M
- UT Houston—$4M/200 patients
- Vanderbilt—$32M
- JK REMAP-CAP—$1M

~$96M Total for CP RCTs

I hope this is useful.

Thanks,
Ashley

From: Wholley, David (FNIH) [T] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=CD9E702FCF28414883D0B6996D677257-WHOLLEYD]
Sent: 7/30/2020 2:16:26 AM
To: Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]; Lane, Cliff (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]; Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Austin, Christopher (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=17597cabc42247548e596778304f781f-austinc]; Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]; Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]
CC: Adam, Stacey (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dcd875f0679648859e1cf101c0943414-adamsj4]
Subject: FW: Do either of you know if DNA is being collected as part of any of the ACTIV-4 antithrombotic trials? Francis Collins wanted to know

Additional context in case helpful. Thanks

From: Hoots, W. Keith (NIH/NHLBI) [E] < (b) (6)
Sent: Wednesday, July 29, 2020 3:54 PM
To: Wholley, David (FNIH) [T] < (b) (6)
Subject: Re: Do either of you know if DNA is being collected as part of any of the ACTIV-4 antithrombotic trials? Francis Collins wanted to know

Dear David,

The plan is for PAX tubes to be collected from participants in all 3 ACTIV IV trials who are enrolled at sites were immediate sample process is feasible— thereby enabling both genomics and transcriptomics to be performed. We do not yet know what percentage of estimated 14K participants this will represent. Budgetary considerations plus logistics will probably determine this final number. I hope this is helpful.

Kindest regards,

Keith

Sent from my iPhone

On Jul 29, 2020, at 2:23 PM, Wholley, David (FNIH) [T] (b) (6) wrote:

David Wholley
Senior Vice-President, Research Partnerships
Foundation for the National Institutes of Health
(b) (6)

fnih.org
11400 Rockville Pike Suite 600 North Bethesda, MD 20852

In 2019, the FNIH earned the highest rating from Charity Navigator for the fifth consecutive year and was recognized as an organization that exceeds industry standards.

From: Tountas Karen (FNIH) [T] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=40C04FEF6F1E46F5B750753CD5A14F93-TOUNTASKH]
Sent: 7/23/2020 9:54:15 AM
To: Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]; Menetsk , Joseph (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5001af52dc4a427ea3d34f1e072f8cb7-menetskijp]
Subject: RE: ACTIV graphics 1.0

Hi Ashley,

Thank you so much for your feedback this is great! I have some additional questions comments intermingled in orange below. Joe, your thoughts before we get too far down this road?

Many thanks!
Karen

From: Parker, Ashley (NIH/OD) [E] < (b) (6)
Sent: Wednesday, July 22, 2020 8:01 PM
To: Tountas, Karen (FNIH) [T] < (b) (6) Menetski, Joseph (FNIH) [T] < (b) (6)
Subject: RE: ACTIV graphics 1.0

One more: ACTIV 4a should be pre-hospitalized (not outpatient asymptomatic) – this should also be added to the population axis.

Thanks!
Ashley

From: Parker, Ashley (NIH/OD) [E]
Sent: Wednesday, July 22, 2020 7:57 PM
To: Tountas, Karen (FNIH) [T] (b) (6) ; Menetski, Joseph (FNIH) [T] (b) (6)
Subject: RE: ACTIV graphics 1.0

Hi Karen,

Th s looks like a great start! A few minor comments/thoughts and responses to your questions:

- Should we keep all drug therapies separate? i.e. place antivirals in a bucket of its own? We would see a sa mon colored dot twice Maybe a so include a bucket for other therapies which will be blank for the moment and include various vaccine treatment options (mRNA, protein, etc.) ?
  KHT: This depends on the approach tracking ACTIV or tracking treatments. We could make a separate list of the drugs and plot them again the phase of the tr al to see how that looks It wouldn't h art to give Franc s a variety of different views to see what he really wants
- think the current model clearly indicates which compounds are being tested in the various population groups – f this was the original request or intent, Joe can confirm based on conversations with Maria and the war room Current graphic doesn't make it clear to know which phase(s) the trials are in although I see the reference target on the bottom r ght. We d scussed the option of showing the trial phases on the x -axis with the patient populations on the y-axis, and compounds on the z -axis but I do not have a preference here.
  KHT I'm still looking into the Z axis - not a possibility in excel - as I like that option the best (so far) For now, made the size of the dots relative to the phase of the trial which I th nk didn't work based on your feedback. 😉
- Should we add additiona' population groups emergency department, hospitalized ventilated vs hospitalized non-ventilated, mild/moderate/severe disease? Only a thought, do we want to track recovery and include

recovered patients eventually in a separate graphic?
KHT: Agreed, but we really need to know the categories/language that all the trials are using and then develop a scale from there. For example, ACTIV-4 has a trial that is hospitalized +/- ventilatory support (based on the NHLBI slide). How granular to we get?

- Should all of the dots be the same size (the salmon dot looks smaller but maybe its my vision!)
  KHT: Nope, not your vision! See comment about my attempt at translating phases above.
- ACTIV-2 – they are starting with their phase 2 study. Subjects will be outpatient – is that outpatient asymptomatic or symptomatic or both? I would assume outpatient symptomatic but Stacey can confirm?
  KHT: I'll ask about this.
- ACTIV-4 – they have three protocols. I think we should track each separately. Your thoughts? Agree we should track them separately and they will launch/start enrollment at different times.
  - Need list of agents to be tested. I am happy to ask NHLBI contacts for this information unless we prefer to start with Stacey?
    KHT: Please as your NHLBI contacts – thanks!
  - Need IND status. In hospital was approved by the DSMB last week. Prehospital will be reviewed by the DSMB today 7/22. I do not know the IND status of the post hospitalization – Stacey will likely have information.
    KHT: I can ask Stacey.
- Need target enrollment numbers for each – I just stuck in numbers for illustrative purposes (see above). I have not seen the target enrollment numbers for ACTIV-4, should we ask Stacey? I am happy to ask NHLBI for ACTIV-4 if needed
  KHT: I'll ask Stacey for ACTIVs 1-3, if you can ask this of the NHLBI folks.
- Need anticipated launch dates for each trial. I've only see launch weeks – ACTIV-2 4 week of July 27 (ACTIV-4 inpatient week of July 27, outpatient and post-hosp. is unclear to me) and ACTIV-1 - mid August
  KHT: This is helpful, I will adjust the data – thanks
- Enrollment tracker looks good to me! No comments at the moment

Please let me know if we should start with Stacey for the remaining responses or if you prefer I contact NHLBI.
KHT: Both as marked above.

Thanks,
Ashley

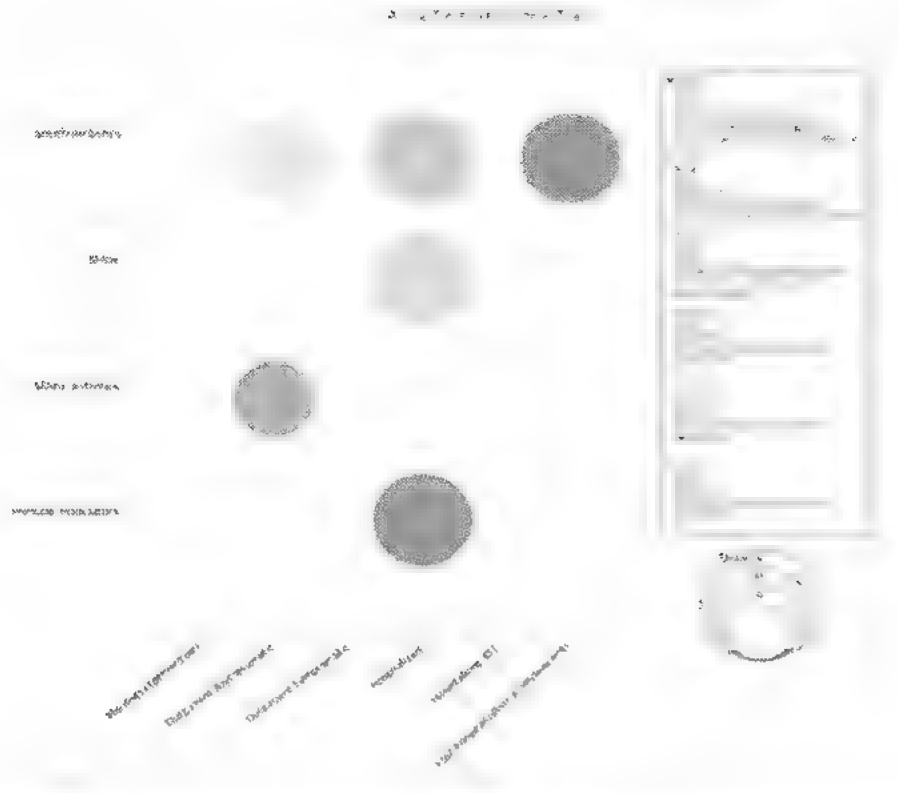
From: Tountas, Karen (FNIH) [T] (b) (6)
Sent: Wednesday, July 22, 2020 5:27 PM
To: Menetski, Joseph (FNIH) [T] < (b) (6) Parker, Ashley (NIH/OD) [E] (b) (6)
Subject: ACTIV graphics 1.0

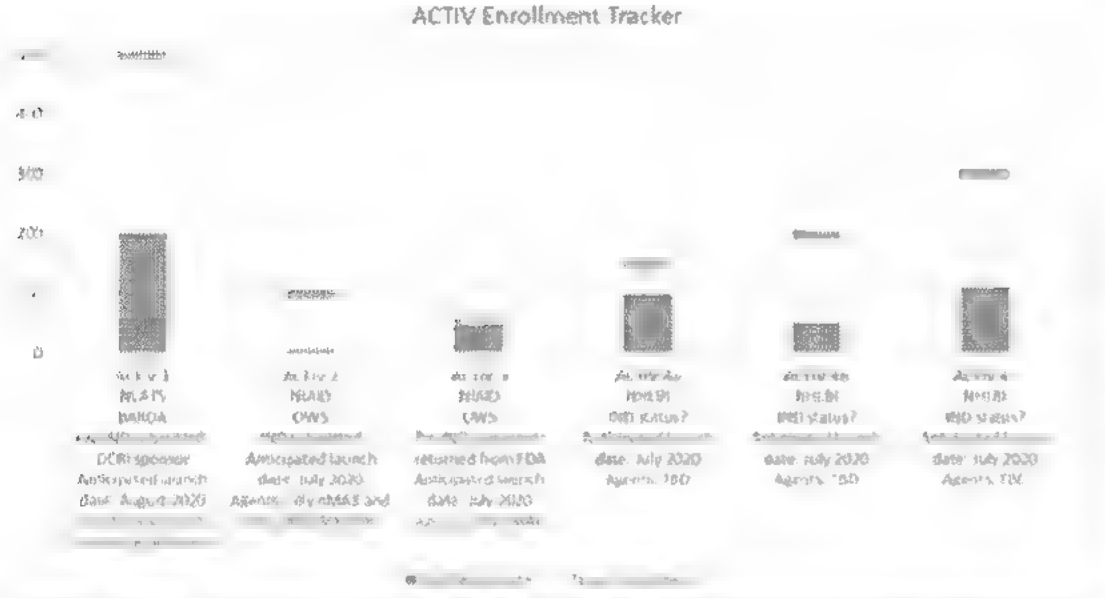
Hi Joe and Ashley,

I have been thinking about graphic representation for the ACTIV CT details and still like what we had talked about this morning, but excel does not all creation of x y/z scatter plots (or at least I cannot figure it out), so …
I made two plots:

- one for information about each trial (I'm a little iffy on this plot, it needs something…),
- and the other to track the status of enrollment versus the target (all numbers are just for demo – I don't have the real enrollment targets and obviously no subjects have enrolled yet.).

See what you think.
Of note, excel would not let me change the axis labels so these are just text boxes – not sure what was going on but. .





Some of the information in the attached spreadsheet needs a bit more granularity as detailed below – do e thei of you have the answers?

- ACTIV-2 – they are starting with their phase 2 study Subjects will be outpatient – is that outpatient asymptomatic or symptomatic or both?
- ACTIV-4 – they have three protocols. I think we should track each separately. Your thoughts?
  - Need list of agents to be tested
  - Need IND status
- Need target enrollment numbers for each – I just stuck in numbers for illustrative purposes (see above)
- Need anticipated launch dates for each trial

Best,

Karen

Karen H. Tountas, PhD
Scientific Program Manager
Foundation for the National Institutes of Health
(b) (6) fnih.org
11400 Rockville Pike, Suite 600, North Bethesda, MD 20852

Donate to the FNIH's Pandemic Response Fund to combat COVID-19: fnih.org/pandemic

From: Tountas Karen (FNIH) [T] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=40C04FEF6F1E46F5B750753CD5A14F93-TOUNTASKH]
Sent: 7/23/2020 12:36:38 PM
To: Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]; Menetsk , Joseph (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5001af52dc4a427ea3d34f1e072f8cb7-menetskijp]
Subject: RE: ACTIV graphics 1.0

Thanks for the feedback. I'll work on some new plots to present.

I think a call would be useful. but my morning is booked. Actually all day is booked until 4. but I can miss some calls. I can make myself available between 1 and 3 or any time after 4.

K

From: Parker, Ashley (NIH/OD) [E] < (b) (6)
Sent: Thursday, July 23, 2020 8:35 AM
To: Menetski, Joseph (FNIH) [T] < (b) (6) Tountas, Karen (FNIH) [T] < (b) (6)
Subject: RE: ACTIV graphics 1.0

I'm available now or 30 mins and then free again at 10am.

Thanks,
Ashley

From: Menetski, Joseph (FNIH) [T] (b) (6)
Sent: Thursday, July 23, 2020 8:32 AM
To: Parker, Ashley (NIH/OD) [E] < (b) (6) Tountas, Karen (FNIH) [T] (b) (6)
Subject: RE: ACTIV graphics 1.0

Lots of great comments.

The goals was to compare therapies, with populations, so I think this y axis on the dot plot is good, but could be separated more, I think.

Can we have another short call? I think there are some things that I am missing. I am not sure the phase of the trial is something that needs to be prominent, more important is the type of therapeutic and the end date.

This may need to be a series of graphs and then they can pick from them??

Joe

From: Parker, Ashley (NIH/OD) [E] < (b) (6)
Sent: Wednesday, July 22, 2020 7:57 PM
To: Tountas, Karen (FNIH) [T] (b) (6) ; Menetski, Joseph (FNIH) [T] (b) (6)
Subject: RE: ACTIV graphics 1.0

Hi Karen,

This looks like a great start! A few minor comments/thoughts and responses to your questions:

- Should we keep all drug therapies separate? i.e. place antivirals in a bucket of its own? We would see a sa mon colored dot twice. Maybe a so include a bucket for other therapies which will be blank for the moment and include various vaccine treatment options (mRNA, protein, etc.) ?
- think the current model clearly indicates which compounds are being tested in the various population groups - if this was the original request or intent, Joe can confirm based on conversations with Maria and the war room. Current graphic doesn't make it clear to know which phase(s) the trials are in although I see the reference target on the bottom r ght. We d scussed the option of showing the trial phases on the x -axis with the patient populations on the y-axis, and compounds on the z -axis but I do not have a preference here
- Should we add additiona population groups, emergency department, hospitalized ventilated vs hospitalized non-ventilated, mild/moderate/severe disease? Only a thought, do we want to track recovery and include recovered patients eventually in a separate graphic?
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    - Need list of agents to be tested I am happy to ask NHLBI contacts for this information unless we prefer to start with Stacey?
    - Need IND status In-hospital was approved by the DSMB last week. Prehospital will be reviewed by the DSMB today 7.22. I do not know the IND status of the post hospitalization Stacey will likely have information.
- Need target enrollment numbers for each – I just stuck in numbers for illustrative purposes (see above) I have not seen the target enrollment numbers for ACTIV -4, shot ld we ask Stacey? I am happy to ask NHLBI for ACTIV-4 if needed
- Need anticipated launch dates for each trial I've only see launch weeks ACTIV 2-4 week of July 27 (ACTIV-4 inpatient week of July 27, outpatient and post hosp. is unclear to me) and ACTIV 1 mid August
- Enrollment tracker looks good to me! No comments at the moment

Please let me know if we should start with Stacey for the remaining responses or if you prefer I contact NHLBI

Thanks,
Ashley

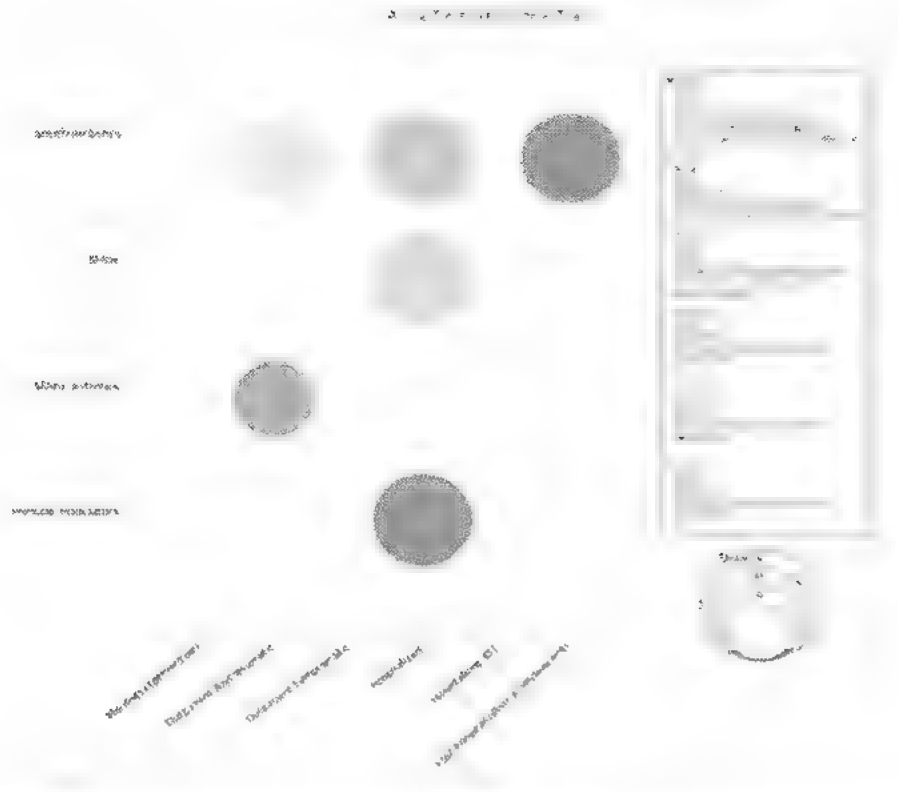
From: Tountas, Karen (FNIH) [T] < (b) (6)
Sent: Wednesday, July 22, 2020 5:27 PM
To: Menetski, Joseph (FNIH) [T] (b) (6) ; Parker, Ashley (NIH/OD) [E] (b) (6)
Subject: ACTIV graphics 1.0

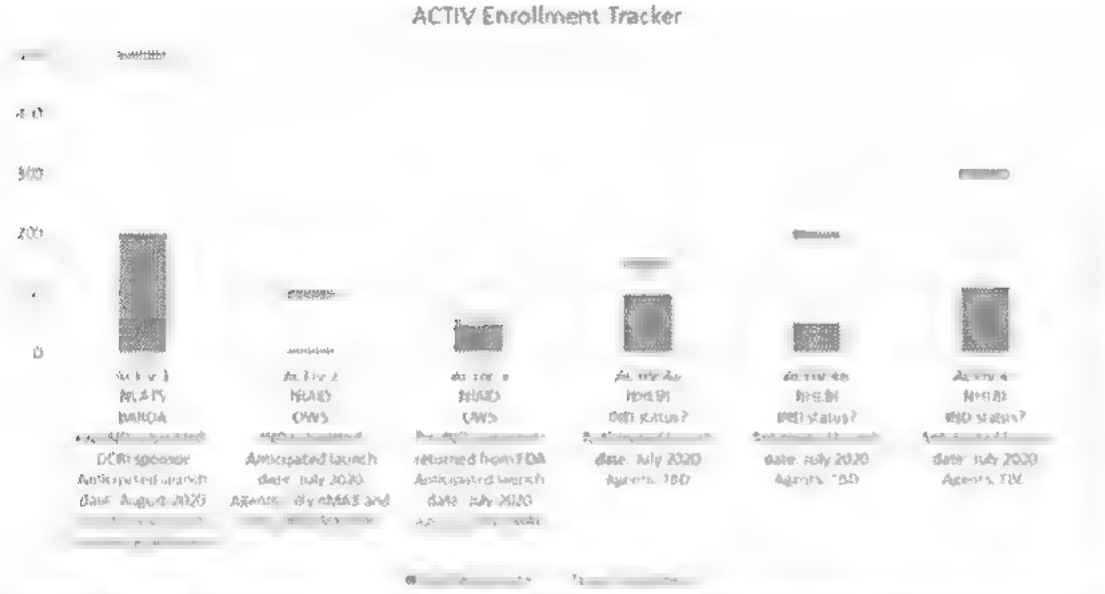
Hi Joe and Ashley,

I have been thinking about graphic representation for the ACTIV CT details and still like what we had talked about this morning, but excel does not al creation of x y z scatter plots (or at least I cannot figure it out), so..
I made two plots:

- one for information abou each trial (I'm a little iffy on this plot, it needs something..).
- and the other to track the status of enrollment versus the target (all numbers are just for demo I don't have the real enrollment targets and obviously no subjects have enrolled yet.).

See what you think.
Of note, excel would not let me change the axis labels so these are just text boxes – not sure what was going on but…





Some of the information in the attached spreadsheet needs a bit more granularity as detailed below – do e thei of you have the answers?

- ACTIV-2 – they are starting with their phase 2 study Subjects will be outpatient – is that outpatient asymptomatic or symptomatic or both?
- ACTIV-4 – they have three protocols. I think we should track each separately. Your thoughts?
  - Need list of agents to be tested
  - Need IND status
- Need target enrollment numbers for each – I just stuck in numbers for illustrative purposes (see above)
- Need anticipated launch dates for each trial

Best,

Karen

Karen H. Tountas, PhD
Scientific Program Manager
Foundation for the National Institutes of Health
(b) (6) fnih.org
11400 Rockville Pike, Suite 600, North Bethesda, MD 20852

Donate to the FNIH's Pandemic Response Fund to combat COVID-19: fnih.org/pandemic

From: Tabak, Lawrence (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=02E22836B5FF4E9988E3770CFC7EE770-TABAKL]
Sent: 6/25/2020 10:36:59 PM
To: Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrat ve Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Austin, Christopher (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=17597cabc42247548e596778304f781f-austinc]
CC: Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]; Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]; Lane, Cliff (NIH/NIA D) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]
Subject: Re: Conversation with Janet Woodcock and Kevin Bugin

Maria,
To write the obvious, FN H has been an enormously important partner in all of these efforts. I am sorry this is causing you so much angst - We will find a way forward one way or another.

Larry

From: "Freire, Maria (FNIH) [T]" < (b) (6)
Date: Thursday, June 25, 2020 at 6:22 PM
To: "Austin, Christopher (NIH/NCATS) [E]" < (b) (6)
Cc: Francis Coll ns < (b) (6) "Tabak, Lawrence (NIH/OD) [E]" < (b) (6) "Wholley, David (FNIH) [T]" < (b) (6) "Anderson, James (NIH/OD) [E]" < (b) (6) "Lane, Cliff (NIH/NIAID) [E]" < (b) (6) "Parker, Ashley (NIH/OD) [E]" < (b) (6)
Subject: Re: Conversation with Janet Woodcock and Kevin Bugin

Yes, absolutely, she certainly is in the crossfire. I'll ask her directly if the FNIH is of any value or not. If we are redundant or if our work is not needed, it would be good to know now and plan accordingly. Thanks again, M.

On Jun 25, 2020, at 6:14 PM, Austin, Christopher (NIH/NCATS) [E] < (b) (6) wrote:

I think that is best. She's clearly under intense pressure from all sides.

From: Freire, Maria (FNIH) [T] < (b) (6)
Sent: Thursday, June 25, 2020 6:06 PM
To: Austin, Christopher (NIH/NCATS) [E] < (b) (6)
Cc: Collins, Francis (NIH/OD) [E] < (b) (6) Tabak, Lawrence (NIH/OD) [E] < (b) (6) Whol ey, David (FNIH) [T] < (b) (6) Anderson, James (NIH/OD) [E] < (b) (6) Lane, Cliff (NIH/NIAID) [E] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6) Kurilla, Michae (NIH/NCATS) [E] < (b) (6) Colvis, Christine (NIH/NCATS) [E] < (b) (6) Bozzette, Sam (NIH/NCATS) [E] < (b) (6) Rutter, Joni (NIH/NCATS) [E] < (b) (6)
Subject: Re: Conversation with Janet Woodcock and Kevin Bugin

Thanks Chris. Very helpful. I'll reach out to Janet directly, then. M.

From: "Austin, Christopher (NIH/NCATS) [E]" (b)
Date: Thursday, June 25, 2020 at 6:04:30 PM
To: "Freire, Maria (FNIH) [T]" (b) (6)
Cc: "Collins, Francis (NIH/OD) [E]" (b) (6) "Tabak, Lawrence (NIH/OD) [E]" (b) (6) "Wholley, David (FNIH) [T]" (b) (6) "Anderson, James (NIH/OD) [E]" (b) (6) "Lane, Cliff (NIH/NIAID) [E]" (b) (6) "Parker, Ashley (NIH/OD) [E]" (b) (6) "Kurilla, Michael (NIH/NCATS) [E]" (b) (6) "Colvis, Christine (NIH/NCATS) [E]" (b) (6) "Bozzette, Sam (NIH/NCATS) [E]" (b) (6) "Rutter, Joni (NIH/NCATS) [E]" (b) (6)
Subject: RE: Conversation with Janet Woodcock and Kevin Bugin

I did but it would need to be tied to the specific activities that are eventually approved under preclinical. I tried to bring up the rolled-up budget with all ACTIV WGs that was submitted 5/23 with the FNIH line item in it, but she was so skeptical of any studies being allowable that I didn't feel I could push it. It was clear that our comprehensive scientific portfolio program approach is not what OWS will support; only individual projects approved one by one. So we will need to support FNIH and NCATS PM by taking from the fixed costs of each individual project.

From: Freire, Maria (FNIH) [T] < (b) (6)
Sent: Thursday, June 25, 2020 5:46 PM
To: Austin, Christopher (NIH/NCATS) [E] (b) (6)
Cc: Collins, Francis (NIH/OD) [E] (b) (6) Tabak, Lawrence (NIH/OD) [E] (b) (6) Wholley, David (FNIH) [T] < (b) (6) Anderson, James (NIH/OD) [E] < (b) (6) Lane, Cliff (NIH/NIAID) [E] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6) Kurilla, Michael (NIH/NCATS) [E] (b) (6) >; Colvis, Christine (NIH/NCATS) [E] (b) (6) ; Bozzette, Sam (NIH/NCATS) [E] (b) (6) >; Rutter, Joni (NIH/NCATS) [E] (b) (6)
Subject: Re: Conversation with Janet Woodcock and Kevin Bugin

Chris, did you bring up any funding for the FNIH? M.

On Jun 25, 2020, at 5.42 PM, Austin, Christopher (NIH/NCATS) [E] (b) (6) wrote:

All,

My team and I just got off the phone with Janet and Kevin. Both the preclinical and ACTIV-1 situations are different than we thought.

Preclinical: the $241M has not been approved beyond the $8.5M for mAb testing that NIAID is doing. The question from Kevin about obligation in 30 days turns out to have been hypothetical To get any of these dollars approved, we will need to make specific arguments to Janet for every compound. No infrastructure, so no $ for BSL3 buildout of primate centers. She thought the 'omics work would be supportable, since it's clinically relevant. The ACTIV prioritization group needs to weight heavily those compounds that need no preclinical work at all, antivirals are much preferred over other MOAs. All compounds have to be in the clinic at latest by December. I told Janet we would come back to her with our list of compounds as soon as the ACTIV Clinical Therapeutics group completes its prioritization, likely ~7/15. Certainly the sooner the better.

ACTIV-1: Janet is not comfortable with the protocol as is, given the RECOVERY dex data (see https://www.medrxiv.org/content/10.1101/2020.06.22.20137273v1 just out), the many other immunomodulators she knows are being tested by companies, and objections she heard DAIT had She wants to see the original evaluation that ACTIV did to select the three compounds, and the written comments from DAIT. She thinks the protocol will likely need to be re-written to account for dex; she brought up again the concept of the "screening trial." To decide what to do, she wants a meeting with her extended group and NCATS, I would want to include NIAID people (Cliff and/or others he would recommend, perhaps even Dan R), and the ACTIV chairs if Janet is willing.

Sorry to give you the sobering news. It was a very different call than I expected. We have a way forward, but we'll need to strategize, particularly wrt the companies in ACTIV-1.

More on our call tomorrow.

Chris

Christopher P. Austin, M.D.
Director

<image001.jpg>

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From: Austin, Christopher (NIH/NCATS) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=17597CABC42247548E596778304F781F-AUSTINC]
Sent: 6/25/2020 9:54:12 PM
To: Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]; Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]; Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Lane, Cliff (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]
CC: Kurilla, Michael (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrat ve Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dc4e85061e3943b9b8ad3f426727861f-mkurilla]; Colvis, Christine (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=4b7e84cce098457896b2df19fa172c87-ccolvis]; Bozzette, Sam (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=85f05a3619cf47c7ae39d7bcf0aac88d-bozzettesaa]; Rutter, Joni (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=157b2517ddb546a8a72844c35eadb062-jrutter]
Subject: RE: Conversation with Janet Woodcock and Kevin Bugin

That's great thanks Jim, very glad to hear.

From: Anderson, James (NIH/OD) [E] < (b) (6)
Sent: Thursday, June 25, 2020 5:48 PM
To: Austin, Christopher (NIH/NCATS) [E] < (b) (6) Collins, Francis (NIH/OD) [E] < (b) (6) Tabak, Lawrence (NIH/OD) [E] < (b) (6) Wholley, David (FNIH) [T] < (b) (6) Freire, Maria (FNIH) [T] < (b) (6) Lane, Cliff (NIH/NIAID) [E] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6)
Cc: Kurilla, Michael (NIH/NCATS) [E] < (b) (6) Colvis, Christine (NIH/NCATS) [E] < (b) (6) Bozzette, Sam (NIH/NCATS) [E] < (b) (6) Rutter, Joni (NIH/NCATS) [E] < (b) (6)
Subject: RE: Conversation with Janet Woodcock and Kevin Bugin

Thanks Chris
We need another supplemental appropriate.
NIAID provided ORIP with $30M for the NPRCs. We are waiting for their admin supplement requests for expanding aBSL facilities, pilot studies of protocols and breeding.

Jim

From: Austin, Christopher (NIH/NCATS) [E] (b) (6)
Sent: Thursday, June 25, 2020 5:42 PM
To: Collins, Francis (NIH/OD) [E] (b) (6) Tabak, Lawrence (NIH/OD) [E] (b) (6) Whol ey, David (FNIH) [T] < (b) (6) Freire, Maria (FNIH) [T] (b) (6) Anderson, James (NIH/OD) [E] < (b) (6) >; Lane, Cliff (NIH/NIAID) [E] (b) (6) >; Parker, Ashley (NIH/OD) [E] < (b) (6)

Cc: Kurilla, Michael (NIH/NCATS) [E] (b) (6) Colvis, Christine (NIH/NCATS) [E] (b) (6) ; Bozzette, Sam (NIH/NCATS) [E] (b) (6) Rutter, Joni (NIH/NCATS) [E] (b) (6)

Subject: Conversation with Janet Woodcock and Kevin Bugin

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Sorry to give you the sobering news. It was a very different call than I expected. We have a way forward, but we'll need to strategize, particularly wrt the companies in ACTIV-1.

More on our call tomorrow.

Chris

Christopher P. Austin, M.D.
Director

National Center for Advancing Translational Sciences

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From: Collins, Francis (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=410E1CA313F44CED9938E50D2FF0B6C2-COLLINSF]
Sent: 6/19/2020 7:56:59 PM
To: Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Austin, Christopher (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=17597cabc42247548e596778304f781f-austinc]; Lane, Cliff (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]; Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]; Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]
Subject: RE: Update on war room discussion this morning

Thanks, David, this is very helpful follow up.
FC

From: Wholley, David (FNIH) [T] < (b) (6)
Sent: Friday, June 19, 2020 1:03 PM
To: Collins, Francis (NIH/OD) [E] < (b) (6) Tabak, Lawrence (NIH/OD) [E] < (b) (6) Austin, Christopher (NIH/NCATS) [E] < (b) (6) Lane, Cliff (NIH/NIAID) [E] < (b) (6) Freire, Maria (FNIH) [T] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6) Anderson, James (NIH/OD) [E] < (b) (6)
Subject: Update on war room discussion this morning

Francis et al:
A couple of updates/answers to questions from this morning's war room meeting:

1) ACTIV-1 Protocol: Stacey Adam confirmed that there has already been a discussion among the ACTIV-1 team members of the implications of dexamethasone, and while there is continued interest in seeing the data it is doubtful the protocol will need serious adjustment even if it becomes standard of care because the protocol is already written to allow for some expected level of site variation, including off-label use of other steroids. The ACTIV-1 team are happy to consider your suggestion that the dexamethasone question may offer something of a premise for further discussions with DAIT, and will look to see more data over the weekend if available. However the real issue is apparently that the companies believe the DAIT immunologists are basing their current objections to the value of the trial on flawed or outdated data on the drugs to be tested. The plan is therefore to hold a discussion with the DAIT folks to discuss the correct data, but do so with the companies present. Because of scheduling conflicts Wednesday is the earliest this can happen; meanwhile the DAIT team is supposed to provide a written answer to ACTIV regarding the request to sponsor the trial in which their objections will be concretely stated. The ACTIV team is not simply waiting for this but pursuing in parallel conversations with both NCATS and CROs. There has already been an Expression of Interest posted on the NCATS portal, and Stacey is working with Sam Bozzette to arrange a webinar with the NCATS investigators next week to explain the trial in further depth.
2) You asked about the sources of data used in the CTC Working Group's site locator dashboard. Karen Tountas confirmed that the dashboard's predictive model combines 7-day rolling inputs on COVID cases and deaths drawn from Johns Hopkins with predictive modeling data from the University of Pennsylvania. The UPenn data, however, though it contains data down to the county level, is only for the U.S. There is apparently a model for predicting international cases on a country level at the Institute for Health Metrics and Evaluation (IHME) at the

University of Washington, but the CTC WG is just starting to look into the feasibility of incorporating it. As discussed this morning re: Dr. Birx's comments at the OWS Board Meeting, the ACTIV dashboard is only a decision-support tool; actual decisions on where to conduct vaccine trials internationally are made via discussions between NIAID and the companies.

David

David Wholley
Senior Vice-President, Research Partnerships
Foundation for the National Institutes of Health
(b) (6)
fnih.org
11400 Rockville Pike Suite 600 North Bethesda, MD 20852

From: Adam, Stacey (FNIH) [T] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=DCD875F0679648859E1CF101C0943414-ADAMSJ4]
Sent: 6/16/2020 12:10:12 PM
To: Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]; Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Austin, Christopher (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=17597cabc42247548e596778304f781f-austinc]; Lane, Cliff (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]; Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]
CC: Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]
Subject: RE: Next wave of antivirals
Attachments: ACTIV-2-Redacted.pdf

Thanks, Jim,

As soon as they are ready, I will send them along. We may be able to send the versions that go to the FDA as early as this week.
In the short-term, I can send you the ACTIV-2 outpatient protocol for mAbs without the drug appendix. This is with FDA now. It may change post their review, which is today or tomorrow, but at least for now it is stable.

Thanks,
Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: (b) (6) | Mobile: (b) (6)

From: Anderson, James (NIH/OD) [E] < (b) (6)
Sent: Tuesday, June 16, 2020 5:45 AM
To: Adam, Stacey (FNIH) [T] < (b) (6) Wholley, David (FNIH) [T] < (b) (6) Austin, Christopher (NIH/NCATS) [E] < (b) (6) Lane, Cliff (NIH/NIAID) [E] < (b) (6) Collins, Francis (NIH/OD) [E] < (b) (6)
Cc: Freire, Maria (FNIH) [T] < (b) (6) Tabak, Lawrence (NIH/OD) [E] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6)
Subject: RE: Next wave of antivirals

Stacey,
That's what I thought. A semi-stable protocol a week from now would be better. Thanks.
Jim

From: Adam, Stacey (FNIH) [T] (b) (6)
Sent: Monday, June 15, 2020 9:56 PM
To: Wholley, David (FNIH) [T] (b) (6) Anderson, James (NIH/OD) [E] (b) (6) Austin, Christopher (NIH/NCATS) [E] < (b) (6) Lane, Cliff (NIH/NIAID) [E] (b) (6) ; Collins, Francis (NIH/OD) [E] (b) (6)
Cc: Freire, Maria (FNIH) [T] (b) (6) ; Tabak, Lawrence (NIH/OD) [E] (b) (6) ; Parker, Ashley (NIH/OD) [E] (b) (6)
Subject: RE: Next wave of antivirals

Hi Jim,

I don't think this shou d be an issue, but a few of our protocols are in pretty constant flux in run up to a first FDA submission that we hope to take place in the next week. Therefore, let me see what the teams are comfortable with at the moment.

Do you need a stable protocol? Or at least would you prefer that? If so, could you wait to the end of the week? We can likely get you something more final then.

If you don't need something stable and are willing to see changes. I can work to get you something tomorrow from ACTIV-1, -2, and -3.

Thanks,
Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: ((b) (6) Mobile: (b) (6)

From: Wholley, David (FNIH) [T] (b) (6)
Sent: Monday, June 15, 2020 9:43 PM
To: Anderson, James (NIH/OD) [E] (b) (6) Austin, Christopher (NIH/NCATS) [E] (b) (6) >; Lane, Cliff (NIH/NIAID) [E] (b) (6) Collins, Francis (NIH/OD) [E] (b) (6)
Cc: Freire, Maria (FNIH) [T] (b) (6) >; Tabak, Lawrence (NIH/OD) [E] (b) (6) >; Parker, Ashley (NIH/OD) [E] < (b) (6) Adam, Stacey (FNIH) [T] (b) (6)
Subject: RE: Next wave of antivirals

None from me. Copying Stacey Adam, who is managing that effort.

From: Anderson, James (NIH/OD) [E] < (b) (6)
Sent: Monday, June 15, 2020 5:57 PM
To: Austin, Christopher (NIH/NCATS) [E] < (b) (6) Lane, Cliff (NIH/NIAID) [E] (b) (6) Collins, Francis (NIH/OD) [E] (b) (6) >
Cc: Wholley, David (FNIH) [T] (b) (6) >; Freire, Maria (FNIH) [T] (b) (6) ; Tabak, Lawrence (NIH/OD) [E] (b) (6) . Parker, Ashley (NIH/OD) [E] (b) (6)
Subject: RE: Next wave of antivirals

Related question: The NPRC staff who are designing the NHP master protocols asked to see the human master protocols. Are there any concerns about this?

Jim

From: Austin, Christopher (NIH/NCATS) [E] (b) (6)
Sent: Monday, June 15, 2020 5:29 PM
To: Lane, Cliff (NIH/NIAID) [E] (b) (6) ; Collins, Francis (NIH/OD) [E] (b) (6)
Cc: Wholley, David (FNIH) [T] (b) (6) ; Freire, Maria (FNIH) [T] (b) (6) ; Tabak, Lawrence (NIH/OD) [E] (b) (6) Anderson, James (NIH/OD) [E] (b) (6) ; Parker, Ashley (NIH/OD) [E] (b) (6)
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Chris

From: Lane, Cliff (NIH/NIAID) [E] (b) (6)
Sent: Monday, June 15, 2020 4:24 PM
To: Collins, Francis (NIH/OD) [E] (b) (6) >
Cc: Wholley, David (FNIH) [T] (b) (6) ; Freire, Maria (FNIH) [T] (b) (6) ; Austin, Christopher (NIH/NCATS) [E] (b) (6) , Tabak, Lawrence (NIH/OD) [E] (b) (6) Anderson, James (NIH/OD) [E] < (b) (6) Parker, Ashley (NIH/OD) [E] (b) (6)
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FC

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Sent: Monday, June 15, 2020 2:05 PM
To: Collins, Francis (NIH/OD) [E] (b) (6)
Subject: RE: Next wave of antivirals

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Sent: Monday, June 15, 2020 1:11 PM
To: Woodcock, Janet < (b) (6)
Cc: Wholley, David N (NIH) (b) (6)
Subject: Next wave of antivirals

Hi Janet,

The Therapeutics-Clinical Working Group of ACTIV is now well into the process of prioritizing the next wave of small molecules, including antivirals. They are planning for these to be rolled into a new *de novo* master protocol, and this trial would become ACTIV-5. I know that your budget, approved by the OWS Board, includes $175M for things like this – but I don't think you and I have talked much about the details. Are you OK with ACTIV proceeding to plan this out, including the master protocol and the clinical trial network that could carry it out? Or do you have other plans such as the I-SPY approach? I wouldn't want the hard working folks at ACTIV to get surprised about the way this might emerge, so I thought I'd best inquire about this now.

David Wholley and I would be glad to talk by phone about this if that would be helpful.

Best, Francis

From: Collins, Francis (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=410E1CA313F44CED9938E50D2FF0B6C2-COLLINSF]
Sent: 6/15/2020 10:40:47 PM
To: Austin, Christopher (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=17597cabc42247548e596778304f781f-austinc]; Lane, Cliff (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]
CC: Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]
Subject: RE: Next wave of antivirals

It definitely sounds as if compounds chosen in Wave 2 need to be ready to go into clinical trials in the next 2 – 3 months, if they are going to be supported by OWS. I assume this decision is coming from Moncef. Maybe we've had a bit of a disconnect here --- I confess that I was assuming all along that Wave 2 was aiming to prior tize compounds ready to go into clinical trials. Otherwise what was the urgency of preparing the *de novo* master protocol for ACTIV-5?

Earlier stage compounds would still be of interest, of course, but we'd have to find some other funding stream for them. Hope springs eternal for the Congress to pass Supplement 5.

Francis

From: Austin, Christopher (NIH/NCATS) [E] < (b) (6)
Sent: Monday, June 15, 2020 5:29 PM
To: Lane, Cliff (NIH/NIAID) [E] < (b) (6) Collins, Francis (NIH/OD) [E] < (b) (6)
Cc: Wholley, David (FNIH) [T] < (b) (6) Freire, Maria (FNIH) [T] < (b) (6) Tabak, Lawrence (NIH/OD) [E] < (b) (6) Anderson, James (NIH/OD) [E] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6)
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FC

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Sent: Monday, June 15, 2020 2:05 PM
To: Collins, Francis (NIH/OD) [E] (b) (6)
Subject: RE: Next wave of antivirals

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To: Woodcock, Janet < (b) (6)
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Best, Francis

From: Wholley, David (FNIH) [T] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=CD9E702FCF28414883D0B6996D677257-WHOLLEYD]
Sent: 6/15/2020 7:39:55 PM
To: Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]; Freire, Mar a (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Austin, Christopher (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=17597cabc42247548e596778304f781f-austinc]; Lane, Cliff (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]; Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]
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Francis·
We have always been prioritizing for everything. This includes repurposed and new drugs—in fact, even drugs that are not ready for the clinic because they require additional preclinical testing; which is why we have a preclinical working group, no? And why our survey seeks information on all candidates.

Having said that, the mix of agents currently in the hopper for consideration run about 80% repurposed, 20% novel, because it is harder to get people to come forward with the latter. We'd be happy to continue whatever mix of activities that you and Janet work out to be appropriate for ACTIV, but do need clarity on the path ahead.
Thanks,
David

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Sent: Monday, June 15, 2020 2:56 PM
To: Wholley, David (FNIH) [T] < (b) (6) Freire, Maria (FNIH) [T] < (b) (6) Austin, Christopher (NIH/NCATS) [E] < (b) (6) Lane, Cliff (NIH/NIAID) [E] < (b) (6) Tabak, Lawrence (NIH/OD) [E] < (b) (6) Anderson, James (NIH/OD) [E] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6)
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Sent: 6/4/2020 5:13:53 PM
To: Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]; Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]; Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Lane, Cliff (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]; Austin, Christopher (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=17597cabc42247548e596778304f781f-austinc]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]
Subject: Re: mAb combinations

Even better.

From: "Anderson, James (NIH/OD) [E]" (b) (6)
Date: Thursday, June 4, 2020 at 1:12 PM
To: "Tabak, Lawrence (NIH/OD) [E]" < (b) (6) Francis Collins < (b) (6) "Wholley, David (FNIH) [T]" < (b) (6) "Freire, Maria (FNIH) [T]" < (b) (6) 'Lane, Cliff (NIH/NIAID) [E]" (b) (6) "Austin, Christopher (NIH/NCATS) [E]" < (b) (6) 'Parker, Ashley (NIH/OD) [E]" < (b) (6)
Subject: RE: mAb combinations

Or just see if they compete using Plasmon Resonance with ag on a fixed surface. Get the Kds as wel l. Larry, I will meet you in the lab.
Jim

From: Tabak, Lawrence (NIH/OD) [E] < (b) (6)
Sent: Thursday, June 4, 2020 12:46 PM
To: Collins, Francis (NIH/OD) [E] < (b) (6) Wholley, David (FNIH) [T] < (b) (6) Freire, Maria (FNIH) [T] < (b) (6) Lane, Cliff (NIH/NIAID) [E] < (b) (6) Austin, Christopher (NIH/NCATS) [E] < (b) (6) Anderson, James (NIH/OD) [E] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6)
Subject: Re: mAb combinations

If you know the epitopes for each Mab, and can perform cryo-EM, and/or molecular simulation, shouldn't you be able to rule out a subset of combinations due to their overlap, and prioritize other combinations? Or is it just easier to "brute force" since there are limited number of combinations?

From: Francis Collins (b) (6)
Date: Thursday, June 4, 2020 at 12:42 PM
To: "Wholley, David (FNIH) [T]" (b) (6) "Freire, Maria (FNIH) [T]" (b) (6) "Lane, Cliff (NIH/NIAID) [E]" (b) (6) "Austin, Christopher (NIH/NCATS) [E]" < (b) (6) "Tabak, Lawrence (NIH/OD) [E]" (b) (6) "Anderson, James (NIH/OD) [E]"

< (b) (6) "Parker, Ashley (NIH/OD) [E]" < (b) (6)
Subject: FW: mAb combinations

Maybe we can discuss this at the War Room....

From: Woodcock, Janet (b) (6)
Sent: Thursday, June 4, 2020 12:38 PM
To: Collins, Francis (NIH/OD) [E] (b) (6) >; Fauci, Anthony (NIH/NIAID) [E] (
Subject: RE: mAb combinations

I would be happy to facilitate getting the abs donated and providing funding for the assays if they can be done. I think this will add to our currently very limited knowledge. jw

From: Collins, Francis (NIH/OD) [E] < (b) (6)
Sent: Wednesday, June 3, 2020 9:03 PM
To: Fauci, Anthony S (NIH) (b) (6) Woodcock, Janet (b) (6)
Subject: FW: mAb combinations

Here's an interesting e-mail thread on ways to approach combinations of mAbs.
FC

From: Graham, Barney (NIH/VRC) [E] (b) (6)
Sent: Wednesday, June 3, 2020 8:19 PM
To: Lane, Cliff (NIH/NIAID) [E] (b) (6)
Cc: Collins, Francis (NIH/OD) [E] (b) (6) ; Sharpless, Norman (NIH/NCI) [E] (b) (6) ; Wholey, David (FNIH) [T] < (b) (6)
Subject: Re: mAb combinations

We hope that in vitro NT is a mechanistic correlate of protection but that has not been definitively proven. It is a reasonable assumption. Would be useful to have in vivo data backing up the assumption.

Barney

Sent from my iPhone

> On Jun 3, 2020, at 7:39 PM, Lane, Cliff (NIH/NIAID) [E] < (b) (6) wrote:
>
> I think it would be a good thing to consider asking the ACTIV pre-clinical group to explore. Not sure of the math!
>
> ---
>
> **From:** "Collins, Francis (NIH/OD) [E]" (b) (6) >
> **Date:** Wednesday, June 3, 2020 at 7:29 PM
> **To:** Barney Graham < (b) (6) "Sharpless, Norman (NIH/NCI) [E]" (. "Lane, Cliff (NIH/NIAID) [E]" (
> **Cc:** "Wholley, David (FNIH) [T]" < (b) (6) b
> **Subject:** RE: mAb combinations
>
> So how much would you trust an in vitro study of neutralization to predict in vivo synergy? Should we try to set that up? Let's say there are 6 mAbs. If I did the math right, you would just need 15 tests to look at all of the binary combinations.

FC

From: Graham, Barney (NIH/VRC) [E] (b) (6)
Sent: Wednesday, June 3, 2020 5:36 PM
To: Sharpless, Norman (NIH/NCI) [E] (b) (6) ; Collins, Francis (NIH/OD) [E] (b) (6) Lane, Cliff (NIH/NIAID) [E] < (b) (6)
Subject: RE: mAb combinations

Our studies in MERS CoV showed that antibodies to some subdomains of spike were more protective than others. This was the case for a certain subset of mAbs to the N-terminal domain (NTD). n addition, some NTD mAbs could synergize (more than additivity) with RBD mAbs and significantly improve dose sparing. Our plans with Abcellera and Lilly has always been to have an RBD and an NTD combination to attack two domains and two mechanisms of action and hopefully achieve synergy and dose-sparing. It may turn out that RBD and neutralization may be sufficient so it seems reasonable to start with that, but more could be done in the background.

RBD is mutable so agree that escape is not likely to occur during acute infection, but on a population level there may be drifting of some sequences. For example, Regeneron's RSV mAb worked against subtype A but the B strains drifted and became resistant, so it was only working for half the problem.

The reasons to use a combination would be to increase potency to achieve dose sparing, to increase breadth in case there is some drift. As Cliff implied from the Ebola story, you would want both mAbs to have efficacy on their own or protection against escape would not occur.

Barney

From: Lane, Cliff (NIH/NIAID) [E] (b) (6)
Sent: Wednesday, June 3, 2020 4:56 PM
To: Collins, Francis (NIH/OD) [E] (b) (6) >; Sharpless, Norman (NIH/NCI) [E] (b) (6) >; Graham, Barney (NIH/VRC) [E] (b) (6)
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I will defer to Barney and Ned but for my 2 cents, I think the only way to do this would be to run a standard in vitro synergy study. It is relatively straight-forward if one had all the relevant antibodies, MTAs, etc. One could prioritize based upon binding sites and IgG isotypes

As you note, in the Ebola studies there was little difference between the single VRC 114 vs. the Regeneron 3-antibody cocktail; whereas the MappBio 3-antibody cocktail was clearly worse. These are both relatively short-course infections (as opposed to HIV). There were a few anecdotes of 114 resistance that have not been confirmed.

I heard the discussion on the ACTIV call and my sense is that it makes the most sense to pursue the single antibody studies in humans while seeing if the pre-clinical ACTIV group could facilitate a donation of antibodies to conduct a classic in vitro synergy study.

Cliff

From: Sharpless, Norman (NIH/NCI) [E] (b) (6)
Sent: Wednesday, June 3, 2020 4:58 PM
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In our phone call last night, Tony thinks Ft. Dietrick would have the capacity. And Janet seems to have the money.

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We have cryo facilities both in MD and at NIEHS. We also have folks who could preform molecular simulations – although DOE may be able to do this more rapidly with their supercomputers.

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Subject: RE: Sorry to be late -- draft presentation for Moncef

Francis,

I would take Janet's counsel very seriously. She has been on the front line, is very supportive of you/NIH on this and knows what will play and what will not. I have not spoken with her but her note is clear: focus on immunomodulators otherwise it looks like you are overreaching.

Cliff is right, NIH already has many trials ongoing. All the more reason to pull the 'portfolio' slide (which I like but maybe not for this) and not shine a light on those. This is about immunomodulators.

If that is the focus, then the discussion is about the phase 2 results: is it wise to wait or not. It seems to me that the goal with Monsef would be to articulate why these are ready to go. I would not touch anything else

My two cents, M.

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I think the slide deck looks good.

I would keep in mind that ACTT-1 (remdesivir vs. placebo); ACTT-2 (remdesivir + baricitinib vs. remdesivir) and 2 IVIg studies (1 inpatient and 1 outpatient) are being supported by NIAID through existing appropriations. ACTT-2 and the two IVIg studies can be considered part of the ACTIV portfolio.

I think there are also studies of hydroxychloroquine (NCATS and NIAID) and immune plasma (NHLBI) being supported by NIH through existing appropriations that are not part of ACTIV.

Cliff

From: "Collins, Francis (NIH/OD) [E]" (b) (6)
Date: Saturday, May 30, 2020 at 8:27 AM
To: "Wholley, David (FNIH) [T]" (b) (6) Lawrence Tabak (b) (6) "Freire, Maria (FNIH) [T]" (b) (6) >, "Austin, Christopher (NIH/NCATS) [E]" (b) (6) , "Lane, Cliff (NIH/NIAID) [E]" (b) (6) "Anderson, James (NIH/OD) [E]" (b) (6) "Parker, Ashley (NIH/OD) [E]" < (b) (6) "Adam, Stacey (FNIH) [T]" < (b) (6)
Subject: FW: Sorry to be late -- draft presentation for Moncef

Very worried about Janet's initial response. Hoping to get us on the same page before 10 am.

From: Collins, Francis (NIH/OD) [E]
Sent: Saturday, May 30, 2020 8:13 AM
To: Woodcock, Janet (b) (6) >
Subject: RE: Sorry to be late -- draft presentation for Moncef

Hi Janet,

I'm actual y quite worried about your reaction – just tried to call to discuss. The five ACTIV trials on the portfolio approach just include the two we are here to discuss, plus monoclonal Abs for inpatients and outpatients, plus a possible next round of antivirals. Aren't those just the main targets for th's "Hail Mary" season of urgency? I would hope that Moncef would see ACTIV as a highly organized cross-sector implementation arm of what needs to happen in the therapeutic part of OWS – not as a threat or a greedy child.

I am glad you are supportive of the anticoagulant trial. But I am very uneasy about backing off and waiting for the company phase II results on immunomodulators – I don't know how far those efforts had gone, and I think they have probably stopped after the ACTIV ExComm endorsement of these compounds to go forward to phase III. Starting those back up again and then waiting for the results seems very likely to lose the opportunity for results by the fall. Aren't we trying to respond to a crisis, even if it means taking some risks and spending money that wouldn't be used this way in normal times? (Compare with vaccines, for instance.) Doesn't the current design of the trial with aggressive analysis of efficacy/futility and safety at 25% enrollment provide a phase II equivalent, and take care of concerns about whether we are moving too fast?

As to costs, the cost for both of these together is still less than 4% of the total of $3B that you had mentioned would be potentially available for therapeutics.

Finally, I won't say this to Moncef – or at least not directly – but I have to say that if OWS rejects out of hand the careful prioritization of the ACTIV team on therapeutic options, I suspect the group will be thoroughly frustrated and demoralized, and may very well decide to disband. They may very well ask you and me why they shou d continue to labor on other things if the results of those labors can be simply discounted by the new czar.

I have my usual COVID-19 Response Team call from 8:30 – 9. I'll try to call you after that, I don't want us to be on different pages when we talk to Moncef at 10.

Francis

From: Woodcock, Janet (b) (6)
Sent: Saturday, May 30, 2020 7:40 AM
To: Collins, Francis (NIH/OD) [E] (b) (6)
Subject: RE: Sorry to be late -- draft presentation for Moncef

Well it is up to you, but the slide on "the portfolio approach" probably won't go over that well. You are basically saying that the ACTIV approach should just be funded. I'd focus for now on the immunomodulators and maybe that you would not launch till the phase 2 data are in hand. The anticoagulants have a very strong rationale and I should be able to get that funded. But appearing to ask for more and more... might be a problem. The higher ups (you are on the Task Force, so you are probably aware) are focusing on OWS as a "Hail Mary" approach that will yield results by the fall If there is a phase 2 signal for one of these molecules then it might put it in that category. jw

From: Collins, Francis (NIH/OD) [E] (b) (6)
Sent: Friday, May 29, 2020 9:06 PM
To: Woodcock, Janet < (b) (6)
Subject: Sorry to be late -- draft presentation for Moncef

Hi Janet,

I hoped to get these to you sooner than 9 pm, but that's the way the week has been going.

Can you have a quick look at slides 1 – 9 and let me know whether these seem like an appropriate set for our meeting with Moncef tomorrow at 10 AM? Any other advice you might have for this conversation would be much appreciated.

Tx, Francis

From: Freire, Maria (FNIH) [T] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=8598D551D1D3455EAF14854C83F41D84-FREIREMC]
Sent: 5/29/2020 2:25:36 AM
To: Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]; Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Lane, Cliff (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]; Austin, Christopher (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=17597cabc42247548e596778304f781f-austinc]; Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]; Fauci, Anthony (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=df38103d75134f658ae2d356f0396b94-afauci]
Subject: Re: URGENT: serious issue for ACTIV therapeutics

OK, I'll let her know the timing - and your thanks. She is fantastic - I'll need to give her a month's vacation, at least!

From: "Collins, Francis (NIH/OD) [E]" (b) (6)
Date: Thursday, May 28, 2020 at 10:22:11 PM
To: "Freire, Maria (FNIH) [T]" (b) (6) "Wholley, David (FNIH) [T]" (b) (6) "Tabak, Lawrence (NIH/OD) [E]" (b) (6) . "Lane, Cliff (NIH/NIAID) [E]" (b) (6) "Austin, Christopher (NIH/NCATS) [E]"("Anderson, James (NIH/OD) [E]" (b) (6) >, "Parker, Ashley (NIH/OD) [E]" (b) (6) "Fauci, Anthony (NIH/NIAID) [E]" < (b) (6)
Subject: RE: URGENT: serious issue for ACTIV therapeutics

Thanks in advance to Stacey. The call with Moncef is now on for Saturday at 10 am. I've also queried Gary Gibbons about questions 6 – 8.

FC

From: Freire, Maria (FNIH) [T] < (b) (6)
Sent: Thursday, May 28, 2020 10:20 PM
To: Collins, Francis (NIH/OD) [E] < (b) (6) Wholley, David (FNIH) [T] < (b) (6) Tabak, Lawrence (NIH/OD) [E] < (b) (6) Lane, Cliff (NIH/NIAID) [E] < (b) (6) Austin, Christopher (NIH/NCATS) [E] < (b) (6) Anderson, James (NIH/OD) [E] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6) Fauci, Anthony (NIH/NIAID) [E] < (b) (6)
Subject: Re: URGENT: serious issue for ACTIV therapeutics

Ah, ok. Stacey is aware you will need this before your call with Moncef on Saturday (or whenever).

From: "Collins, Francis (NIH/OD) [E]" (b) (6)
Date: Thursday, May 28, 2020 at 10.14:45 PM
To: "Freire, Maria (FN H) [T]" < (b) (6) "Wholley, David (FNIH) [T]" < (b) (6) 'Tabak, Lawrence (NIH/OD) [E]" (b) (6) , "Lane, Cliff (NIH/NIAID) [E]" (b) (6) >, "Austin, Christopher (NIH/NCATS) [E]" (b) (6) "Anderson, James (NIH/OD) [E]" (
b
Subject: RE: URGENT: serious issue for ACTIV therapeutics

I think he wrote the document.

From: Freire, Maria (FNIH) [T] (b) (6)
Sent: Thursday, May 28, 2020 10:13 PM
To: Collins, Francis (NIH/OD) [E] (b) (6) Wholley, David (FNIH) [T] < (b) (6) Tabak, Lawrence (NIH/OD) [E (b) (6) >; Lane, Cliff (NIH/NIAID) [E] < (b) (6) Austin, Christopher (NIH/NCATS) [E] (b) (6) Anderson, James (NIH/OD) [E] (b) (6) ; Parker, Ashley (NIH/OD) [E] (b) (6) Fauci, Anthony (NIH/NIAID) [E] (b) (6)
Subject: Re: URGENT: serious issue for ACTIV therapeutics

OK, this is complicated but we'll give you the details you need. I believe we can answer most of your questions.

On the positive side, he seems open to discussing this, which is good. M.

P.S. Did he say where he got the document?

From: "Collins, Francis (NIH/OD) [E]" (b) (6)
Date: Thursday, May 28, 2020 at 9:49:54 PM
To: "Wholley, David (FNIH) [T]" (b) (6) , "Freire, Maria (FNIH) [T]" (b) (6) 'Tabak, Lawrence (NIH/OD) [E]" (b) (6) >, "Lane, Cliff (NIH/NIAID) [E]" (b) (6) "Austin, Christopher (NIH/NCATS) [E]" (b) (6) "Anderson, James (NIH/OD) [E]" < (b) (6) "Parker, Ashley (NIH/OD) [E]" (b) (6) "Fauci, Anthony (NIH/NIAID) [E]" (b) (6)
Subject: URGENT: serious issue for ACTIV therapeutics

Houston, we have a problem.

In the OWS Board meeting at 5 PM, Moncef spent most of the time talking about vaccines. No real surprises there except Novavax is under consideration for the second tier – I hadn't heard that before.

Then in the last 15 minutes he got into therapeutics. He spoke from the attached document. Most of the emphasis was on convalescent plasma, IVIg, and mAbs. As you will see, the reference to immunomodulators and anticoagulants sounds quite vague. It got worse – in the oral presentation, he referred to these as proof-of-concept. It would be fine for NIH to study these, he said, and if there appeared to be some possible benefit, then (and only then) OWS could be consulted.

I jumped in to say there had been a misunderstanding, these were intended to be phase III trials and were endorsed unanimously by the ACTIV ExComm as the highest priorities for hospitalized patients. We were ready to ask for OWS support now. Janet was also on the phone, and backed me up on that. Moncef expressed surprise that the immunomodulators would go straight to phase III without smaller studies first –

and Debbie Birx unhelpfully suggested that the companies must love having all this work done for them that they would never spend their own money on.

It was really uncomfortable. Ultimately the decision was that Moncef and I needed to work this out separately. As you can see, he is proposing to meet tomorrow. The times he is proposing won't work for me, so I plan to ask him for a call on Saturday. But I'll need to be prepared for that.

So I'll need answers to the following questions:

1. For the immunomodulators, what's the status of the protocol?
2. The companies have agreed to provide drugs, right? Do they have any other "skin in the game"?
3. What's the counterargument to Moncef's view that these repurposed compounds should first go through phase II?
4. What about a proposal to run a phase II/III, would that satisfy all of the concerns? (That's what Janet suggests.)
5. With no network currently lined up to take on the immunomodulators, is the $70M estimate still correct? Will the need to use CROs make this more expensive?
6. For the three different anticoagulants (on hospitalized patients), what's the current status of the protocol?
7. Is PETAL all set to initiate this? How soon?
8. I know we put $40M in the OWS budget for this – if that doesn't come through, is NHLBI prepared to fund it?

Let's discuss at the War Room meeting tomorrow AM. David and I might be slightly late if the AMP Ex Comm meeting runs late.

FC

From: moncef slaoui (b) (6)
Sent: Thursday, May 28, 2020 9:07 PM
To: Collins, Francis (NIH/OD) [E] (b) (6)
Subject: Re: Hoping to follow up soon

Dear Francis
Thank you for your note
Yes I am sorry I misunderstood and frankly was surprised that companies would agree to go straight into Phase 3 without clear rational or evidence for expected benefit (and lack of harm).
It is important to be clear that they need to have skin in the game rather than a free try .
I look forward to a good to a good scientific discussion Francis. As for all other areas my aim is to help support and speed availability of medicines and vaccines for patients.
I can talk tomorrow between 10:30 and 12 or 1:30 and 3pm
I hope one of these can work
Please let me know

With my best regards

Moncef

On May 28, 2020, at 8:47 PM, Collins, Francis (NIH/OD) [E] < (b) (6) wrote:

Hi Moncef,

I'm truly sorry about the confusion today relating to the Phase III readiness of the immunomodulator and anticoagulant trials that have been given top priority by ACTIV. I need to pull all of the deta ls together to give you a full briefing. Might we be able to talk tomorrow sometime? Or this weekend?

Many thanks for all the amazing progress you have made in less than two weeks!

Best, Francis

From: Wholley, David (FNIH) [T] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=CD9E702FCF28414883D0B6996D677257-WHOLLEYD]
Sent: 5/27/2020 8:25:25 PM
To: Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]; Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Adam, Stacey (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dcd875f0679648859e1cf101c0943414-adamsj4]; Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Austin, Christopher (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=17597cabc42247548e596778304f781f-austinc]; Lane, Cliff (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]; Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]
Subject: RE: Message

Francis,
I consulted with Stacey. The answer is : We are designing the mAb master protocols to be as agent agnostic as possible so we could bring in single agent and combos there if needed (both mAb and other types of agents). We are assuming the mAbs will need to be done in combination with each other eventually for full effect. These are both Phase II to III adaptive progressive trials with moderately aggressive efficacy and futility reviews to allow for early stopping both in Phase II and III if needed.

We can create another protocol, but we would want to make sure we have learned from all the lessons on these first trials as far as logistics.

Feel free to pass that on to Mikael.

-----Original Message-----
From: Collins, Francis (NIH/OD) [E] < (b) (6)
Sent: Wednesday, May 27, 2020 3:10 PM
To: Wholley, David (FNIH) [T] < (b) (6) Freire, Maria (FNIH) [T] < (b) (6) Adam, Stacey (FNIH) [T] < (b) (6) Tabak, Lawrence (NIH/OD) [E] < (b) (6) Austin, Christopher (NIH/NCATS) [E] < (b) (6) Lane, Cliff (NIH/NIAID) [E] < (b) (6) Anderson, James (NIH/OD) [E] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6)
Subject: FW: Message

Interesting reflection from Dolsten about possible combination studies. Adding Stacey.

-----Original Message-----
From: (b) (6)
Sent: Wednesday, May 27, 2020 8:49 AM
To: Collins, Francis (NIH/OD) [E] < (b) (6) Woodcock, Janet (FDA/CDER) (b) (6)
Cc: FMedSci Trevor < (b) (6)
Subject: Message

Good morning again

Thanks for your participation this morning in HEVER warm up

One reflection from our dialogue thay we touched briefly on

1 The master protocols will be very important as an alternative to small studies and allowing rapid identifications of well performing compounds in well designed studies . Picking the winners early and terminating less attractive studies .

2 We also discussed that several large companies (Biotech or Pharma) do most often run well powered RCT P2 studies and can do it swiftly either independently proves joining master protocols if they are on a similar time table

3 One bridge between 1 & 2 may be an option to test drug combinations from different sources or study patient sub groups allowing to share an all comer patient group and then stratify into subgroups selected for possibly different treatment protocols . How much do we see this as additional value of the master protocol ? We start to see significant heterogeneity in Covid disease and at some time point we may realize that there isn't just one single silver bullet...but rather combinations . Does the strategy for the master protocol or ACTIV punctuate combinations and in the future different subsets of Covid sufficiently ?

4 I still worry that the scientific insights about medical, cellular and molecular characteristics on corona virus disease is superficial due to its fragmentation of knowledge and much dark space remaining The risk is that we hope for quick wins by many shots at goal but having poor visibility on more guided shots in goal leads to just partial progress .

Hopefully Francis and all of is will find a path similar to AMP to bring deeper insights on the Coronavirus species , it's impact on humans and key other hosts that leads to science winning the end game

Welcome your thoughts and advice
(b) (6)

Sent from my iPhone

From: Austin, Christopher (NIH/NCATS) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=17597CABC42247548E596778304F781F-AUSTINC]
Sent: 5/27/2020 7:31:14 PM
To: Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]; Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Adam, Stacey (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dcd875f0679648859e1cf101c0943414-adamsj4]; Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Lane, Cliff (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]; Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]
Subject: RE: Message

Mikael's point 4ff is why we added omics studies on the clinical materials gathered in trials to the OWS preclinical proposal, a la AMP.

-----Original Message-----
From: Collins, Francis (NIH/OD) [E] < (b) (6)
Sent: Wednesday, May 27, 2020 3:10 PM
To: Wholley, David (FNIH) [T] < (b) (6) Freire, Maria (FNIH) [T] < (b) (6) Adam, Stacey (FNIH) [T] < (b) (6) Tabak, Lawrence (NIH/OD) [E] < (b) (6) Austin, Christopher (NIH/NCATS) [E] < (b) (6) Lane, Cliff (NIH/NIAID) [E] < (b) (6) Anderson, James (NIH/OD) [E] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6)
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From: (b) (6) (b) (6)
Sent: Wednesday, May 27, 2020 8:49 AM
To: Collins, Francis (NIH/OD) [E] < (b) (6) Woodcock, Janet (FDA/CDER) < (b) (6)
Cc: FMedSci Trevor < (b) (6)
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Good morning again

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Welcome your thoughts and advice
(b) (6)

Sent from my iPhone

Sent: 10/15/2020 11:42:20 AM
To: Walsh, Elizabeth (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f182b2c69fc94c0e813b762a8f2fbf13-walsher]; Schwetz, Tara (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=0b1da1e9650d44fa9a9e2d94f24b5035-schwetzta]
CC: Brodd, Lauren (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=ba665dea08e54171b3d6890c2518ddb9-leponelm]
Subject: RE: ACTIV COVID-19 Clinical and Preclinical Compound Portal

Hi Tara and Beth,

I have new news. Lauren Brodd and I are working closely with OCPL to review and provide updates to the ACTIV website and we noticed the link to the ACTIV portal is publicly available as of 9/10. The ACTIV working group pages were posted at the end of last week and this update included the link to the ACTIV clinical and preclinical portal/RedCap survey approved by FNIH. The ACTIV portal currently lives on the Preclin.ca WG page and Clinical Tx WG page.

Apologies for not noticing this sooner! (hence my original question to the war room) – this question was in the draft but was later approved and found today during our weekly review.

Tara – if you agree, I will follow up with the war room tomorrow morning to let them know the ACTIV portal is live and we are working with your team to ensure the submission processes are clearly defined and synched?

Beth – for the irrelevant content coming through the NIH portal, would it be useful to have all general submissions routed directly to ES and only have the serious inquiries for diagnostics, vaccines, technologies reviewed by the cross-NIH team? It may require having a click system for general inquiries, vaccines, diagnostics that leads to a series of targeted questions to weed out the irrelevant submissions although I understand this creates more work! Sighs! 😔 The current platform could be too easy and potentially invites those types of general submissions which is fine but seems more appropriate for ES to sort.

Below are a few options for consideration knowing we would need to consult OCPL for any changes to the ACTIV website once we have a clear path forward. These are only ideas but defer to your team if there are other recommendations.

- **Option 1: Do nothing and continue the triage process for ACTIV via OD and then send to FNIH to send the ACTIV/RedCap survey**
  - **Pros:**
    - Current process in place for companies interested in submitting compounds to ACTIV without completing the longer ACTIV/RedCap survey.
  - **Cons:**
    - Now two portals for preclinical and clinical therapeutic submissions which could be confusing to users
    - Selected companies routed to ACTIV currently submit information twice (NIH portal and ACTIV/RedCap) although the ACTIV/RedCap survey takes longer.
    - Interested companies go through several channels before receiving email with ACTIV/RedCap link that is now available on the ACTIV website.
- **Option 2: Ask OCPL to add the ACTIV/RedCap link to the main ACTIV webpage "submit your ideas" (for companies who want to submit preclinical or clinical therapeutic compounds) and keep the existing link to NIH portal (for companies who want to submit vaccines, other). Make any necessary edits to the current ACTIV language provided on the NIH portal.**
  - **Pros:**
    - Interested companies can submit preclinical and clinical therapeutics directly to ACTIV without going through the NIH portal and triage process to receive the l nk,

- Any submissions to the NIH portal that should go to ACTIV can be directed to complete the ACTIV/RedCap link on the website.
- Should limit the number of therapeutic submissions to the NIH portal – limit the number for review and triage.
- Any follow up questions regarding submissions to ACTIV/RedCap can be directed to FNIH agent prioritization leads for response.

- **Cons:**
  - Links to 2 different portals could be confusing to users if not clearly defined.
  - Providing link to NIH portal (diagnostics, technologies, vaccines, others) on the ACTIV webpage could be confusing given there is no agent prioritization role for ACTIV beyond therapeutics.

- **Option 3: Ask OCPL to remove the existing NIH portal link from the ACTIV website and replace with ACTIV/RedCap link. Make any necessary edits to the current ACTIV language provided on the NIH portal.**
  - **Pros:**
    - One link available for ACTIV submissions may avoid confusion.
    - Interested companies can submit preclinical and clinical therapeutics directly to ACTIV agent information without going through the NIH portal and triage process to receive the link.
    - Any submissions to the NIH portal that should go to ACTIV can be directed to complete the ACTIV/RedCap link on the website.
    - Should limit the number of therapeutic submissions to the NIH portal – limit the number for review and triage.
    - Vaccines, diagnostics, others continue to come to the NIH portal via one location NIH COVID page.
  - **Cons:**
    - ACTIV/RedCap may potentially receive compounds beyond therapeutics (vaccines, diagnostics, others) not relevant for ACTIV

Thanks,
Ashley

From: Walsh, Elizabeth (NIH/OD) [E] < (b) (6)
Sent: Tuesday, September 15, 2020 6:23 AM
To: Schwetz, Tara (NIH/OD) [E] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6)
Subject: Re: ACTIV COVID-19 Clinical and Preclinical Compound Portal

Hi Tara and Ashley,

For context, 593 of 724 submissions to date have been labeled as preclinical, therapeutic, or "other". I've passed submissions from each of these categories on to ACTIV in the past. Of the 593 submissions, about 20% were approved for dissemination by the review group, and still fewer were appropriate for ACTIV, somewhere between 10% and 15%.

Once the portal was public for a few weeks, we started to receive and have continued to receive a lot of irrelevant content (e.g., anecdotal stories, Fauci/Collins fan mail, and questions that need to be redirected to other channels). These types of responses are the bulk of what is received through the portal now, and it can take a significant amount of time for someone to go through them.

Best,
Beth

From: "Schwetz, Tara (NIH/OD) [E]" (b) (6) >
Date: Monday, September 14, 2020 at 11:31 PM
To: "Parker, Ashley (NIH/OD) [E]" <(b) (6)
Cc: "Walsh, Elizabeth (NIH/OD) [E]" (b) (6) >
Subject: Re: ACTIV COVID-19 Clinical and Preclinical Compound Portal

The clarity is definitely a big piece to consider. Additionally, we are still receiving quite a number of submissions that we would not have any interest in moving forward with (low quality/scientific rigor). What I don't know is how many of these are tx vs. vx, dx, or other. My guess is the tx submissions are a good chunk of these. Looping in Beth to confirm though.

Best,

Tara A. Schwetz, PhD
Associate Deputy Director, NIH
A: Building 1, Room 138
P: 301-402-3965 | **M:** 301-538-4920

From: "Parker, Ashley (NIH/OD) [E]" (b) (6)
Date: Monday, September 14, 2020 at 11:24 PM
To: Tara Schwetz <tara. (b) (6)
Subject: Re: ACTIV COVID-19 Clinical and Preclinical Compound Portal

To my understanding, the goal for making the ACTIV portal/RedCap survey public is to allow companies direct access to submit detailed information about "therapeutic" compounds — this information is needed for the ACTIV prioritization process.

The ACTIV portal is specifically for preclinical and clinical therapeutics but nothing else. Vaccines, diagnostics, and other general submissions are not appropriate.

I agree — having two portals is already somewhat confusing and companies who are vetted through the NIH portal may feel confused after receiving a follow-up email to complete the ACTIV survey for a therapeutic compound they've already submitted. If ACTIV wants to move forward with making the link public maybe we'll need a "click here to submit a preclinical or clinical therapeutic agent to ACTIV/FNIH" with link to RedCap on the ACTIV website and NIH portal page but would need a "click here for vaccines, diagnostics, other technologies to link to the NIH portal and edit ACTIV language?" Renate will likely have better ideas!

I have no preference here but agree the process should be streamlined and easy for a submitter to understand. It's also tough to manage the changing landscape —ACTIV initially accepted vaccine candidates but now defer to NIAID now that the Vaccines WG ceased operations as of July 31st and currently meet on an ad hoc basis.

Please let me know if you need any additional info.

Thanks,
Ashley

On Sep 14, 2020, at 9:55 PM, Schwetz, Tara (NIH/OD) [E] (b) (6) > wrote:

OK, thanks. What is the goal of making the ACTIV portal public? Are the WGs wanting to invite broad submission? We'll have to discuss how best to link and communicate this, as I do worry this could get confusing to people.

Best,

Tara A. Schwetz, PhD
Associate Deputy Director, NIH
A: Building 1, Room 138
P: (b) (6) | M: (b) (6)

<image001.png>

From: "Parker, Ashley (NIH/OD) [E]"(
Date: Monday, September 14, 2020 at 6:19 PM
To: Tara Schwetz < (b) (6)
Subject: RE: ACTIV COVID-19 Clinical and Preclinical Compound Portal

Hi Tara,

For background, there have been discussions about whether or not the ACTIV portal developed by the ACTIV preclinical and clinical WGs and NCATS should be made public on the ACTIV website This is independent of the NIH portal and submissions process although we can discuss options for streamlining if ACTIV decides to make it public

I didn't think we needed to discuss any efforts to streamline/sync the efforts beyond the ongoing process before knowing if ACTIV would like to make this available or continue to send as "invite only." I planned to touch base with you and Beth after knowing what decision ACTIV decides to move forward with but please let me know if you have any questions.

Thanks,
Ashley

From: Parker, Ashley (NIH/OD) [E]
Sent: Monday, September 14, 2020 12:37 PM
To: Tabak, Lawrence (NIH/OD) [E] (b) (6) Collins, Francis (NIH/OD) [E] (b) (6) Wholley, David (FNIH) [T] (b) (6) ; Freire, Maria (FNIH) [T] < (b) (6) Austin, Christopher (NIH/NCATS) [E] (b) (6)
Cc: Gadbois, Ellen (NIH/OD) [E] (b) (6) >; Schwetz, Tara (NIH/OD) [E] (b) (6)
Subject: RE: ACTIV COVID-19 Clinical and Preclinical Compound Portal

Also, the N H portal (not specific to ACTIV but includes RADx, others) was put in place several months before the ACTIV portal was developed. They are only synched with the NIH portal submissions vetted for ACTIV receiving a link to complete the ACTIV survey.

From: Parker, Ashley (NIH/OD) [E]
Sent: Monday, September 14, 2020 12:33 PM
To: Tabak, Lawrence (NIH/OD) [E] (b) (6) >; Collins, Francis (NIH/OD) [E] (b) (6) Wholley, David (FNIH) [T] (b) (6) ; Freire, Maria (FNIH) [T] (b) (6) Austin, Christopher (NIH/NCATS) [E] (b) (6)
Cc: Gadbois, Ellen (NIH/OD) [E] (b) (6) Schwetz, Tara (NIH/OD) [E] (b) (6) >
Subject: RE: ACTIV COVID 19 Clinical and Preclinical Compound Portal

Not related. The information submitted to the ACTIV portal is used for the WGs to prioritize compounds and contains detailed information. The NIH portal has very limited information about the compounds, not sufficient for the agent prioritization process.

No issues with proprietary information as submitters must provide consent.

Hopefully this is helpful context.

Thanks,
Ashley

From: Tabak, Lawrence (NIH/OD) [E] (b) (6)
Sent: Monday, September 14, 2020 12:28 PM
To: Parker, Ashley (NIH/OD) [E] < (b) (6) Collins, Francis (NIH/OD) [E] (b) (6) >; Wholley, David (FNIH) [T] (b) (6) Freire, Maria (FNIH) [T] (b) (6) ; Austin, Christopher (NIH/NCATS) [E] (b) (6)
Cc: Gadbois, Ellen (NIH/OD) [E] < (b) (6) . Schwetz, Tara (NIH/OD) [E] (b) (6) >
Subject: Re: ACTIV COVID-19 Clinical and Preclinical Compound Portal

How does this relate to the NIH portal? I thought they were synched up. Are there still proprietary concerns? (cc'ing Tara who has dealt with that issue for NIH portal).

From: "Parker, Ashley (NIH/OD) [E]" (b) (6)
Date: Monday, September 14, 2020 at 12:21 PM
To: Francis Collins (b) (6) >, "Tabak, Lawrence (NIH/OD) [E]" (b) (6) ., "Wholley, David (FNIH) [T]" (b) (6) "Freire, Maria (FNIH) [T]' (b) (6) "Austin, Christopher (NIH/NCATS) [E]" < (b) (6)
Cc: "Gadbois, Ellen (NIH/OD) [E]" < (b) (6)
Subject: ACTIV COVID-19 Clinical and Preclinical Compound Portal

Hi All,

If we have time on Wednesday, could we discuss if ACTIV would like to make the ACTIV COVID-19 Clinical and Preclinical Compound Portal also known as the RedCap survey public? The link to the ACTIV portal is currently shared via email to submitters who are vetted through the NIH COVID 19 Candidate and Technologies Portal and when companies send emails to Francis, Janet, FNIH, etc. to inquire about submitting their compound(s) for ACTIV.

This question was raised a while ago and was recently brought to my attention for follow-up.

Thanks,
Ashley

Sent: 6/5/2020 2:20:59 PM
To: Adam, Stacey (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dcd875f0679648859e1cf101c0943414-adamsj4]
Subject: RE: 170 Candidate Spreadsheet

Hi Stacey,

No worries, I will not share but want to compare the list with others listed in the OWS slides. I saw a note from Moncef asking FC to look at other candidates listed in the OWS slides by BARDA and DOD and I thought most of them were already evaluated by ACTIV.

David will likely if not already follow up with you on this – quick yes/no below. Not sharing but wanted to know.

(b) (4)

From: Adam, Stacey (FNIH) [T] < (b) (6)
Sent: Friday, June 5, 2020 10:14 AM
To: Parker, Ashley (NIH/OD) [E] < (b) (6)
Subject: RE: 170 Candidate Spreadsheet

Hi Ashley,

Attached is our Triage Tracker that started out with the 170 agents Please do not share as this is still rough. We haven't had time to clean it up and make it pretty and we were moving fast at the time. Also, it names reviewers for compound and I would not want that to get out to the public.

If you have any questions, I would be happy to discuss it with you.

Thanks,
Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: (b) (6) | Mobile (b) (6)

From: Parker, Ashley (NIH/OD) [E] < (b) (6)
Sent: Friday, June 5, 2020 7:31 AM

To: Adam, Stacey (FNIH) [T] < (b) (6)
Subject: 170 Candidate Spreadsheet

Hi Stacey,

Do you have the list of prioritized compounds handy in a spreadsheet? – not to be shared but I am interested in reviewing the list.

Thanks,
Ashley

Sent: 6/26/2020 7:38:05 AM
To: Rashid, Kamilah (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=58ce52e57bb74034834aa8660b5c8677-rashidkl], Walsh, Elizabeth (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f182b2c69fc94c0e813b762a8f2fbf13-walsher]
Subject: RE: P ease Review: BARDA Corona Watch | Therapeutic Candidates for Consideration
Attachments: RE: BARDA Corona Watch | Therapeutic Candidates for Consideration ; ACTIV Emails Queries rv 052120.xlsx

Hi Kamilah,

I responded to Christine and have not heard anything – please see attached.

From: Rashid, Kamilah (NIH/OD) [E] < (b) (6)
Sent: Wednesday, May 27, 2020 4:34 PM
To: Parker, Ashley (NIH/OD) [E] < (b) (6) Walsh, Elizabeth (NIH/OD) [E] < (b) (6)
Subject: Please Review: BARDA Corona Watch | Therapeutic Candidates for Consideration

Hi Ashley and Beth,

I am working to finalize responses to the questions Ashley forwarded me from NCATS. I did an initial passthrough with responses in red and Tara responded in purple.

1. Merge relevant information from all portals mapped to consistent data fields into the N H db ("relevant" means subm ssions relevant to the ACTIV process; some NIH portals will contain COVID-related but not ACTIV-relevant entries)
    a. OD received submissions (prior to implementation of portal) – ***Ashely***, do you have this spreadsheet and have the data fields already been aligned with BARDA and/or the NIH portal?
        i. Response: No, backfilling of OD received submissions has not occurred at this time but will happen over the upcoming weeks. The data is being pu led from all the subm ssions/reach-outs that were forwarded to DDRMS.
        {Question: are we going to do this for the ACTIV spreadsheet that Ashley has to back-fill that information as well? What has been discussed? I don't know how big it is or how easy it is to align the data, but we may wish to do that. We will also want to denote the ones that came in through Ashley's spreadsheet and through DDRMS.}

    b. NIAID submissions – spreadsheet provided by Alan Embry (contact him to ensure on same page); data fields need to be mapped/aligned
    {Denote these too. Also, let's do this on our end – they are swamped and the last thing they need to do is figure out spreadsheet columns}

2. Send email to those not submitted through the NIH porta
    Questions: I think they maybe referring to the drafting of a generic message as a submission receipt? think clarity is needed because we do not intend to reach out to applicants.
    {We have already reached out, where appropriate, to people who were sent to DDRMS. Before that, some people (ICDs) were randomly (or seemingly) responding to requests. I think we let those alone and start a clean slate with the portal.}

    a. Permission to integrate into ACTIV prioritization ***{???}***

    b. Fill out survey – ***either compound RedCap survey or NIH portal depending on answer to initial question – thinking it's the former?***

Response: Do not think this question is directed towards us, more so of an internal NCATS question.
{OK. I'm not familiar with the RedCap survey. I didn't know they made one, but maybe this is what FNIH/Deloitte has done…}

Below are questions that I have that I'm hoping both of you can help answer:

- **Bullet (1a)**: Do we plan to back-fill the submissions that Ashley has received? I know that we briefly discussed this at some point, but want to confirm. If so, Ashley, do you anticipate that it will be easy to align the responses with the portal spreadsheet? Please see the questions asked by Tara. I don't think it's necessary – the submission were shared with the ACTIV working groups each week and they follow-up on those which were of interest. We collected basic information and it does not contain the level of detail outlined in the portal - see attached.

- **Bullet (1b):** Beth, I know that you previously mentioned that Alan from NIAID would be sharing a spreadsheet, is he sharing directly with you and on what cadence? Also, does the spreadsheet align with portal fields?

- **Bullet (2a):** Ashley, I think we will need some clarity on what NCATS is asking to do here, unless you have any insight? Not clear to me either.

- **Bullet (2B):** Ashley, are you familiar with any involvement by FNIH/Deloitte to create the RedCap survey?

The attached email contains all of Tara's feedback.

Thank you!

Best,
Kamilah

Kamilah Rashid, PharmD
Health Science Policy Analyst
Immediate Office of the Director
National Institutes of Health
One Center Drive
Building 1, Room 114
Bethesda, MD 20892
M: (b) (6)
P: (b) (6)
E: (b) (6)

From: "Parker, Ashley (NIH/OD) [E]" < (b) (6)
Date: Wednesday, May 20, 2020 at 5:27 PM
To: "Rashid, Kamilah (NIH/OD) [E]" (b) (6)
Subject: FW: BARDA Corona Watch | Therapeutic Candidates for Consideration

From: Cutillo, Christine (NIH/NCATS) [E] (b) (6)
Sent: Wednesday, May 20, 2020 3:37 PM
To: Adam, Stacey (FNIH) [T] (b) (6) Parker, Ashley (NIH/OD) [E] (b) (6) Anderson, James (NIH/OD) [E] < (b) (6)

Cc: Austin, Christopher (NIH/NCATS) [E] < (b) (6) Santangelo, George (NIH/OD) [E]
(b) (6) Ford-Scheimer, Stephanie (NIH/NCATS) [C] (b) (6)
Subject: RE: BARDA Corona Watch | Therapeutic Candidates for Consideration

Dear All,

Wanted to provide you with an update – we have been working with Andrew Derr (Deloitte NIH contract) to get someone by tomorrow/end of the week to start working on this. More detailed steps are included below in addition to a few questions. For clarification – which spreadsheet/database contains the appropriate data fields that should be propagated/mapped for each of the others (e.g., the BARDA submissions or the ACTIV compound spreadsheet)? I believe the NIH portal was built based on the BARDA submission data fields, but if we're ultimately aiming to connect to the ACTIV compound spreadsheet then potentially we should build toward that now when connecting these unsolicited submissions. Also, where do the submissions received via the NIH portal live and/or will a spreadsheet be sent at some periodicity? I apologize if these are questions that have already been addressed, but I haven't received that information yet.

Best,
Christine

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1. Merge relevant information from all portals mapped to consistent data fields into the N H db ("relevant" means subm ssions relevant to the ACTIV process; some NIH portals will contain COVID-related but not ACTIV-relevant entries)
    a. BARDA submissions – ***is this the template of data fields that all others should be aligned with or should they be aligned with the data fields contained within the ACTIV compound spreadsheet?***
    b. OD received submissions (prior to implementation of portal) – ***Ashely***, do you have this spreadsheet and have the data fields already been aligned with BARDA and/or the NIH portal?
    c. NIAID submissions – spreadsheet provided by Alan Embry (contact him to ensure on same page); data fields need to be mapped/aligned
    d. NCATS submissions – data fields need to be mapped/aligned
2. Eliminate duplicate entries (sent by the same person to multiple portals)
    a. Via name/email matching
3. Send email to those not submitted through the NIH porta
    a. Permission to integrate into ACTIV prioritization
    b. Fill out survey – ***either compound RedCap survey or NIH portal depending on answer to initial question – thinking it's the former?***
4. Collate all into single db/spreadsheet for ACTIV/TransNIH use
5. Set up process for updating submissions received via N H portal and other sources
    a. ***Where do the submissions received via the NIH portal live and/or will a spreadsheet be sent at some periodicity?***
    b. ***Has an email been sent out alerting folks at NIH to direct external inquiries to this portal or do we need to set up a process for receiving new submissions from e.g., NIAID?***

Christine Cutillo, MMCi
Special Assistant to the Director
Office of the Director
National Center for Advancing Translational Sciences
National Institutes of Health
Phone: (b) (6)
(b) (6)

From: Austin, Christopher (NIH/NCATS) [E] (b) (6)
Sent: Sunday, May 17, 2020 12:37 PM
To: Adam, Stacey (FNIH) [T] < (b) (6) Parker, Ashley (NIH/OD) [E] (b) (6) ; Cutillo, Christine (NIH/NCATS) [E] (b) (6) ; Ford-Scheimer, Stephanie (NIH/NCATS) [C] (b) (6) ; Anderson, James (NIH/OD) [E] < (b) (6) Santangelo, George (NIH/OD) [E] (b) (6)
Subject: FW: BARDA Corona Watch | Therapeutic Candidates for Consideration

All,

We made good headway last week on a strategy to eliminate redundant entries from different submission portals to enable a complete and nonredundant list of entries to be provided to Stacey's group for wave 2 and wave 3 prioritization. The list from BARDA enclosed, and the analysis Stacey did on it, is just the kind of information we have, or need to extract, from the NIAID portal, NCATS portal, Bldg 1 portal, intramural portal, and nonpublic OPA db. The steps defined are:

1. Merge relevant information from all portals into the NIH db ("relevant" means submissions relevant to the ACTIV process; some NIH portals will contain COVID-related but not ACTIV-relevant entries)
2. Eliminate duplicate entries (sent by the same person to multiple portals) by name/email matching
3. Depending on whether the portal required the submitter to grant permission for sharing internal to NIH and/or with ACTIV (latter, non-NIH for evaluation purposes only, under NDA), send submitter an email ask ng for such permission to be granted, and
4. Depending on whether the submitter included the fields needed by Stacey's group for initial evaluation, in same email ask the submitter to supply the missing information
5. Collate responses and deliver to Stacey.

Christine, please devise a sequential workflow and enlist those you need for help.

Many thanks to all the portal owners for helping to create a filter funnel that will get the relevant information to ACTIV.

Chris

From: Adam, Stacey (FNIH) [T] (b) (6)
Sent: Saturday, May 16, 2020 11:05 AM
To: Freire, Maria (FNIH) [T] (b) (6) Collins, Francis (NIH/OD) [E] (b) (6)
Cc: Parker, Ashley (NIH/OD) [E] (b) (6) ; Tabak, Lawrence (NIH/OD) [E] (b) (6) Lane, Cliff (NIH/NIAID) [E] (b) (6) >; Austin, Christopher (NIH/NCATS) [E] < (b) (6) Anderson, James (NIH/OD) [E] (b) (6) >; Wholley, David (FNIH) [T] < (b) (6)
Subject: RE: BARDA Corona Watch | Therapeutic Candidates for Consideration

Hi Maria,

Of the top three candidates we selected: Abatacept (CTLA-IgG1 Fusion), Cenicriviroc (CCR2/5 inhhibitor), and infliximab (TNF-alpha antagonist). Only the TNF inhibition seems to appear on the BARDA list.

Of our top 39 candidates that got scored, many MOAs were working to address some of the same issues that those on the BARDA list seem to target, such as anticoagulants, though those we reviewed and selected were largely already available in hospitals so they could we easily and quick deployed for the NHLBI/NINDS trial. BARDA's anticoagulants seem to be next generation and working through slightly different MOAs. Also, we had number of anti-inflammatory targeting MOAs on our list that don't appear on the BARDA list, such as anti-IL17, RASP inhibition, PDE4 nhibition, GSMF

inhibition, and others. But again, both groups trying to get at the same issue, just through different points in the inflammation pathway. The one thing I notice is the BARDA list only seems to have 1 antiviral on their list, whereas we have about 9, and while we didn't prioritize them first, we did think some would likely be high priority for our next wave of trials with a slightly different design.

Again, I hope this is helpful.

Thanks,
Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: (b) (6) | Mobile: (b) (6)

From: Freire, Maria (FNIH) [T] (b) (6)
Sent: Saturday, May 16, 2020 10:51 AM
To: Adam, Stacey (FNIH) [T] < (b) (6) Collins, Francis (NIH/OD) [E (b) (6)
Cc: Parker, Ashley (NIH/OD) [E] (b) (6) ; Tabak, Lawrence (NIH/OD) [E] (b) (6) ; Lane, Cliff (NIH/NIAID) [E] (b) (6) ; Austin, Christopher (NIH/NCATS) [E] (b) (6) ; Anderson, James (NIH/OD) [E] (b) (6) Wholley, David (FNIH) [T] (b) (6)
Subject: Re: BARDA Corona Watch | Therapeutic Candidates for Consideration

Thank Stacey- very helpful. How about the converse: are there MOA on the WG list that are not on this one? M.

From: "Adam, Stacey (FNIH) [T]" (b) (6)
Date: Saturday, May 16, 2020 at 9:40:55 AM
To: "Freire, Maria (FN H) [T]' (b) (6) . "Collins, Francis (NIH/OD) [E]" (b) (6)
Cc: "Parker, Ashley (N H/OD) [E]" (b) (6) "Tabak, Lawrence (NIH/OD) [E]" (b) (6) "Lane, Cliff (NIH/NIAID) [E]" (b) (6) "Austin, Christopher (NIH/NCATS) [E]" < (b) (6) "Anderson, James (NIH/OD) [E]' (b) (6) "Wholley, David (FNIH) [T]" (b) (6)
Subject: RE: BARDA Corona Watch | Therapeutic Candidates for Consideration

Hi Maria and Francis,

As these compounds largely did not have information in the public domain for ongoing trials or major preclinical experiments in SARS-CoV-2 when we did our first pull 5 weeks ago, most, if not all, would not have been on our list.

However, looking at the mechanisms of action (MOA), we did have a number of agents that have same or similar MOAs, including IL-6 inhibition (3 agents on our review list) and JAK/STAT inhibitors (4 on our list). Both of these classes our group chose not to select for the first large confirmatory trial we were designing because their MOAs were being studied in well designed trials by other groups.

There are some MOAs that were not on our original list, such at IL-15 inhibition, though we did have many other IL inhibitors, including IL-1, 6, and 17. The Syk inhibitors are also a new MOA that did not appear in the first 170 of clinically ready agents

I hope this information helps.

Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: (b) (6) , Mobile: (b) (6)

From: Freire, Maria (FNIH) [T] (b) (6)
Sent: Saturday, May 16, 2020 10:03 AM
To: Collins, Francis (NIH/OD) [E] (b) (6)
Cc: Parker, Ashley (NIH/OD) [E] (b) (6) >; Tabak, Lawrence (NIH/OD) [E] (b) (6) >; Lane, Cliff (NIH/NIAID) [E] (b) (6) , Austin, Christopher (NIH/NCATS) [E] (b) (6) ; Anderson, James (NIH/OD) [E] (b) (6) >; Wholley, David (FNIH) [T (b) (6) Adam, Stacey (FNIH) [T] (b) (6) >
Subject: Re: BARDA Corona Watch | Therapeutic Candidates for Consideration

Good morning Stacey. Could you please take a look and let us know? Many thanks, M.

On May 16, 2020, at 8:46 AM, Collins, Francis (NIH/OD) [E] (b) (6) wrote:

Interesting. Wou d the therapeutics on this list have been on the list of 170 that the Therapeutics Clinical WG was prioritizing?

FC

From: Parker, Ashley (NIH/OD) [E] (b) (6) >
Sent: Friday, May 15, 2020 2:49 PM
To: Collins, Francis (NIH/OD) [E] < (b) (6) Tabak, Lawrence (NIH/OD) [E] (b) (6) >; Lane, Cliff (NIH/NIAID) [E] (b) (6) Austin, Christopher (NIH/NCATS) [E] (b) (6) ; Anderson, James (NIH/OD) [E (b) (6) >; Wholley, David (FNIH) [T] (b) (6) Freire, Maria (FNIH) [T] (b) (6)
Cc: Adam, Stacey (FNIH) [T] (b) (6)
Subject: BARDA Corona Watch | Therapeutic Candidates for Consideration

Hi all,

Attached is a list of compounds shared by one of NIAID's program officers, Steve Smiley who is a reviewer/participant assigned to the **therapeutics Tech Watch (now CoronaWatch) meetings** at BARDA. Steve indicated they have ~10 meetings per week and there are other NIAID experts who join these. He suggested NIH reps who attend the BARDA meetings could assists with sharing compounds with ACTIV – recent focus has been on therapeutic products for infected outpatients for the DAIDS ACTG network but he indicated many products are better suited to phase 2 testing in hospitalized patients.

Steve also suggested we develop a short script for the NIH POCs who attend the BARDA Corona Watch meetings and use this as an opportunity to inform companies about ACTIV We could link them to our vetting process (e new portal) and/or feed them directly to the working groups. It seems prior to ACTIV, NIAID has used these Corona watch meetings to look for opportunities that would be useful for NIAID networks Cliff likely has more insight here. The opportunity to expand and be inclusive of ACTIV seems like the right path and an opportunity to stay connected with what comes through BARDA.

Would this be something of interest to the group?

Thanks,

Ashley

From: Parker, Ashley (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=306B2244466140FAA95AAAAFE06EBD70-PARKERAS]
Sent: 5/20/2020 11:12:08 PM
To: Cutillo, Christine (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c04c8f5063c34361bb7491f216f75adc-cutilloc]; Adam, Stacey (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dcd875f0679648859e1cf101c0943414-adamsj4]; Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]
CC: Austin, Christopher (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=17597cabc42247548e596778304f781f-austinc]; Santangelo, George (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3dc0ef5ad44247ffb31d8f3abff01fe4-santangelog]; Ford-Scheimer, Stephanie (NIH/NCATS) [C] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a43f1ad78f5045ba83edd30f906845dc-fordscheime]; Gladman, Jordan (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=eb38a598f96f488299a655a7312138fd-gladmanjt]
Subject: RE: BARDA Corona Watch | Therapeutic Candidates for Consideration

Hi Christine,

There have been a few updates since the note from Chris on Sunday and I want to clarify a few things.

- We have not received any spreadsheets from BARDA with data fields – one of the NIAID POs who is a reviewer for the BARDA CoronaWatch meetings shared a PDF short list of compounds for ACTIV Tx clinical WG to consider – this is what I shared on Friday.
- The spreadsheet OD has managed prior to the launch of the COIVD portal only contains emails (contact info, brief descriptor i.e. vaccine, preclinical interest, etc.) Dr. Collins has received as it relates to ACTIV. We have shared these with FNIH each week to sort and share relevant information with the WGs. ES has sent a standard response to those emails and in some cases FNIH has followed up when relevant. I think only a handful may have been fully useful and fleshed out.
- Tara's team is leading the NIH portal efforts – yes, data fields are closely aligned with BARDA. Also, Tara's team has a review process for queries received through this portal and would have the spreadsheet of data fields you are looking for – it may be a good idea to touch base with Tara and her team to ensure the efforts outlined below are aligned.
- **As of yesterday, my understanding was Dr. Tabak made a decision to coordinate these efforts via a small IC data group and next steps are to bring in PM from Deloitte as you've indicated below to access all of the needs including RADx, ACTIV, and others before making a final decision to merge information from all portals. My take on this was to pause for the moment but I defer to Chris on the action items below.**

I hope this is useful.

Best,
Ashley

From: Cutillo, Christine (NIH/NCATS) [E] < (b) (6)
Sent: Wednesday, May 20, 2020 3:37 PM
To: Adam, Stacey (FNIH) [T] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6) Anderson, James (NIH/OD) [E] < (b) (6)
Cc: Austin, Christopher (NIH/NCATS) [E] < (b) (6) Santangelo, George (NIH/OD) [E]

< (b) (6) Ford-Scheimer, Stephanie (NIH/NCATS) [C] < (b) (6)
Subject: RE: BARDA Corona Watch | Therapeutic Candidates for Consideration

Dear All,

Wanted to provide you with an update - we have been working with Andrew Derr (Deloitte NIH contract) to get someone by tomorrow/end of the week to start working on this. More detailed steps are included below in addition to a few questions. For clarification – which spreadsheet/database contains the appropriate data fields that should be propagated/mapped for each of the others (e.g., the BARDA submissions or the ACTIV compound spreadsheet)? I believe the NIH portal was built based on the BARDA submission data fields, but if we're ultimately aiming to connect to the ACTIV compound spreadsheet then potentially we should build toward that now when connecting these unsolicited submissions. Also, where do the submissions received via the NIH portal live and/or will a spreadsheet be sent at some periodicity? I apologize if these are questions that have already been addressed, but I haven't received that information yet.

Best,
Christine

---

1. Merge relevant information from all portals mapped to consistent data fields into the N H db ("relevant" means subm ssions relevant to the ACTIV process; some NIH portals will contain COVID-related but not ACTIV-relevant entries)
    a. BARDA submissions – ***is this the template of data fields that all others should be aligned with or should they be aligned with the data fields contained within the ACTIV compound spreadsheet?***
    b. OD received submissions (prior to implementation of portal) – ***Ashely***, do you have this spreadsheet and have the data fields already been aligned with BARDA and/or the NIH portal?
    c. NIAID submissions – spreadsheet provided by Alan Embry (contact him to ensure on same page); data fields need to be mapped/aligned
    d. NCATS submissions – data fields need to be mapped/aligned
2. Eliminate duplicate entries (sent by the same person to multiple portals)
    a. Via name/email matching
3. Send email to those not submitted through the NIH portal
    a. Permission to integrate into ACTIV prioritization
    b. Fill out survey – ***either compound RedCap survey or NIH portal depending on answer to initial question – thinking it's the former?***
4. Collate all into single db/spreadsheet for ACTIV/TransNIH use
5. Set up process for updating submissions received via N H portal and other sources
    a. ***Where do the submissions received via the NIH portal live and/or will a spreadsheet be sent at some periodicity?***
    b. ***Has an email been sent out alerting folks at NIH to direct external inquiries to this portal or do we need to set up a process for receiving new submissions from e.g., NIAID?***

Christine Cutillo, MMCi
Special Assistant to the Director
Office of the Director
National Center for Advancing Translational Sciences
National Institutes of Health
Phone (b) (6)
(b) (6)

NIH NCATS: COLLABORATE. INNOVATE. ACCELERATE.

From: Austin, Christopher (NIH/NCATS) [E] (b) (6)
Sent: Sunday, May 17, 2020 12:37 PM
To: Adam, Stacey (FNIH) [T] (b) (6) >; Parker, Ashley (NIH/OD) [E] (b) (6) >; Cutillo, Christine (NIH/NCATS) [E] (b) (6) >; Ford-Scheimer, Stephanie (NIH/NCATS) [C] (b) (6) (b) (6) Anderson, James (NIH/OD) [E] (b) (6) Santangelo, George (NIH/OD) [E] < (b) (6)
Subject: FW: BARDA Corona Watch | Therapeutic Candidates for Consideration

All,

We made good headway last week on a strategy to eliminate redundant entries from different submission portals to enable a complete and nonredundant list of entries to be provided to Stacey's group for wave 2 and wave 3 prioritization. The list from BARDA enclosed, and the analysis Stacey did on it, is just the kind of information we have, or need to extract, from the NIAID portal, NCATS portal, Bldg 1 portal, intramural portal, and nonpublic OPA db. The steps defined are:

1. Merge relevant information from all portals into the NIH db ("relevant" means submissions relevant to the ACTIV process; some NIH portals will contain COVID-related but not ACTIV-relevant entries)
2. Eliminate duplicate entries (sent by the same person to multiple portals) by name/email matching
3. Depending on whether the portal required the submitter to grant permission for sharing internal to NIH and/or with ACTIV (latter, non NIH for evaluation purposes only, under NDA), send submitter an email ask ng for such permission to be granted, and
4. Depending on whether the submitter included the fields needed by Stacey's group for initial evaluation, in same email ask the submitter to supply the missing information
5. Collate responses and deliver to Stacey.

Christine, please devise a sequential workflow and enlist those you need for help.

Many thanks to all the portal owners for helping to create a filter funnel that will get the relevant information to ACTIV.

Chris

From: Adam, Stacey (FNIH) [T] (b) (6)
Sent: Saturday, May 16, 2020 11:05 AM
To: Freire, Maria (FNIH) [T] (b) (6) ; Collins, Francis (NIH/OD) [E] (b) (6)
Cc: Parker, Ashley (NIH/OD) [E] (b) (6) >; Tabak, Lawrence (NIH/OD) [E (b) (6) Lane, Cliff (NIH/NIAID) [E] (b) (6) ; Austin, Christopher (NIH/NCATS) [E] <: (b) (6) Anderson, James (NIH/OD) [E] < (b) (6) Wholley, David (FNIH) [T] (b) (6)
Subject: RE. BARDA Corona Watch | Therapeutic Candidates for Consideration

Hi Maria,

Of the top three candidates we selected: Abatacept (CTLA-IgG1 Fusion), Cenicriviroc (CCR2/5 inhhibitor), and infliximab (TNF-alpha antagonist). Only the TNF inhibition seems to appear on the BARDA list.

Of our top 39 candidates that got scored, many MOAs were working to address some of the same issues that those on the BARDA list seem to target, such as anticoagulants, though those we reviewed and selected were largely already available in hospitals so they could we easily and quick deployed for the NHLBI/NINDS trial. BARDA's anticoagulants seem to be next generation and working through slightly different MOAs. Also, we had number of anti-inflammatory targeting MOAs on our list that don't appear on the BARDA list, such as anti-IL17, RASP inhibition, PDE4 nhibition, GSMF inhibition, and others. But again, both groups trying to get at the same issue, just through different points in the

inflammation pathway. The one thing I notice is the BARDA list only seems to have 1 antiviral on their list, whereas we have about 9, and while we didn't prioritize them first, we did think some would likely be high priority for our next wave of trials with a slightly different design.

Again, I hope this is helpful.

Thanks,
Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: (b) (6) | Mobile: (b) (6)

From: Freire, Maria (FNIH) [T] (b) (6)
Sent: Saturday, May 16, 2020 10:51 AM
To: Adam, Stacey (FNIH) [T] (b) (6) ; Collins, Francis (NIH/OD) [E] (b) (6)
Cc: Parker, Ashley (NIH/OD) [E] < (b) (6) Tabak, Lawrence (NIH/OD) [E] (b) (6)
Lane, Cliff (NIH/NIAID) [E] (b) (6) , Austin, Christopher (NIH/NCATS) [E] (b) (6)
Anderson, James (NIH/OD) [E] (b) (6) >; Wholley, David (FNIH) [T] (b) (6)
Subject: Re: BARDA Corona Watch | Therapeutic Candidates for Consideration

Thank Stacey- very helpful. How about the converse. are there MOA on the WG list that are not on this one? M.

From: "Adam, Stacey (FNIH) [T]' (b)
Date: Saturday, May 16, 2020 at 9:40:55 AM
To: "Freire, Maria (FNIH) [T]" < (b) (6) "Collins, Francis (NIH/OD) [E]" < (b) (6)
Cc: "Parker, Ashley (NIH/OD) [E]" < (b) (6) >, "Tabak, Lawrence (NIH/OD) [E]' (b) (6)
"Lane, Cliff (NIH/NIAID) [E]" (b) (6) "Austin, Christopher (NIH/NCATS) [E]" (b) (6)
"Anderson, James (NIH/OD) [E]" < (b) (6) "Wholley, David (FNIH) [T]' (b) (6)
Subject: RE: BARDA Corona Watch | Therapeutic Candidates for Consideration

Hi Maria and Francis,

As these compounds largely did not have information in the public domain for ongoing trials or major preclinical experiments in SARS-CoV-2 when we did our first pull 5 weeks ago, most, if not all, would not have been on our list

However, looking at the mechanisms of action (MOA), we did have a number of agents that have same or similar MOAs, including IL-6 inhibition (3 agents on our review list) and JAK/STAT inhibitors (4 on our list) Both of these classes our group chose not to select for the first large confirmatory trial we were designing because their MOAs were being studied in well designed trials by other groups.

There are some MOAs that were not on our original list, such at IL-15 inhibition, though we did have many other IL inhibitors, including IL-1, 6, and 17. The Syk inhibitors are also a new MOA that did not appear in the first 170 of clinically ready agents.

I hope this information helps.

Stacey

Stacey J. Adam, PhD

Director, Cancer
Research Partnerships
Direct: (b) (6) Mobile: (b) (6)

From: Freire, Maria (FNIH) [T] (b) (6)
Sent: Saturday, May 16, 2020 10:03 AM
To: Collins, Francis (NIH/OD) [E] (b) (6) >
Cc: Parker, Ashley (NIH/OD) [E] (b) (6) >; Tabak, Lawrence (NIH/OD) [E (b) (6)
Lane, Cliff (NIH/NIAID) [E] (b) (6) , Austin, Christopher (NIH/NCATS) [E] (b) (6)
Anderson, James (NIH/OD) [E] (b) (6) Wholley, David (FNIH) [T] (b) (6) Adam,
Stacey (FNIH) [T] (b) (6)
Subject: Re: BARDA Corona Watch | Therapeutic Candidates for Consideration

Good morning Stacey. Could you please take a look and let us know? Many thanks, M.

On May 16, 2020, at 8:46 AM, Collins, Francis (NIH/OD) [E] (b) (6) · wrote:

Interesting. Wou d the therapeutics on this list have been on the list of 170 that the Therapeutics Clinical WG was prioritizing?

FC

From: Parker, Ashley (NIH/OD) [E] < (b) (6)
Sent: Friday, May 15, 2020 2:49 PM
To: Collins, Francis (NIH/OD) [E] < (b) (6) Tabak, Lawrence (NIH/OD) [E] (b) (6) ; Lane,
Cliff (NIH/NIAID) [E] < (b) (6) Austin, Christopher (NIH/NCATS) [E] (b) (6) >; Anderson,
James (NIH/OD) [E] (b) (6) Wholley, David (FNIH) [T] (b) (6) Freire, Maria (FNIH)
[T] (b) (6)
Cc: Adam, Stacey (FNIH) [T] < (b) (6)
Subject: BARDA Corona Watch | Therapeutic Candidates for Consideration

Hi all,

Attached is a list of compounds shared by one of NIAID's program officers, Steve Smiley who is a reviewer/participant assigned to the **therapeutics Tech Watch (now CoronaWatch) meetings** at BARDA. Steve indicated they have ~10 meetings per week and there are other NIAID experts who join these. He suggested NIH reps who attend the BARDA meetings could assists with sharing compounds with ACTIV – recent focus has been on therapeutic products for nfected outpatients for the DAIDS ACTG network but he indicated many products are better suited to phase 2 testing in hospitalized patients.

Steve also suggested we develop a short script for the NIH POCs who attend the BARDA Corona Watch meetings and use this as an opportunity to inform companies about ACTIV. We could link them to our vetting process (.e. new portal) and/or feed them directly to the working groups. It seems prior to ACTIV, NIAID has used these Corona watch meetings to look for opportunities that would be useful for NIAID networks Cliff likely has more insight here. The opportunity to expand and be inclusive of ACTIV seems like the right path and an opportunity to stay connected with what comes through BARDA.

Would this be something of interest to the group?

Thanks,

Ashley

From: Collins, Francis (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=410E1CA313F44CED9938E50D2FF0B6C2-COLLINSF]
Sent: 2/10/2021 3:59:40 PM
To: Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]
CC: Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrat ve Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Adam, Stacey (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dcd875f0679648859e1cf101c0943414-adamsj4]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]
Subject: RE: ACTIV-6 Budget Estimate

This looks great, David. I don't think I will want to shorten it.

Now I just need to get with Tony to organize the whole menu of research needs, and then we will bring this to Kessler.

FC

From: Wholley, David (FNIH) [T] < (b) (6)
Sent: Wednesday, February 10, 2021 7:58 AM
To: Collins, Francis (NIH/OD) [E] < (b) (6)
Cc: Freire, Maria (FNIH) [T] < (b) (6) Adam, Stacey (FNIH) [T] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6)
Subject: FW: ACTIV-6 Budget Estimate

Francis:
Here s a 4-pager that includes protocol summary, schema, timeline, study assumptions and estimated budget. We were not sure exactly which elements would go into your "2-pager" and thought you might want more detail to impress Kessler that this has been well thought through. You can select out of this those elements you need to get it into the shape you desire. Copying Ashley.
Thanks, David

From: Adam, Stacey (FNIH) [T] (b) (6)
Sent: Tuesday, February 9, 2021 7:49 PM
To: Wholley, David (FNIH) [T] (b) (6) Freire, Maria (FNIH) [T] < (b) (6)
Subject: RE: ACTIV-6 Budget Estimate

Hi David,

I will see what we can do on estimated accrual per site and estimated number of sites that we can open each week That is what we will need to get to those numbers. I am not sure if we have a sense of this yet.

As for the write-up that FC requested, I know that he wanted 2 pages or less, but take a look at this protocol summary, schema, timeline (same as below), study assumptions, and estimated budget based on assumptions. It is 4 pages, but I think it would show Kessler's team that we have already thought this through pretty deeply. Is it too much?

Thanks,
Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: (b) (6) Mobile: (b) (6)

From: Wholley, David (FNIH) [T] (b) (6)
Sent: Tuesday, February 9, 2021 7:16 PM
To: Adam, Stacey (FNIH) [T] (b) (6) Freire, Maria (FNIH) [T] (b) (6)
Subject: RE: ACTIV-6 Budget Estimate

Looks good, but he's going to ask also about the first agent. Assuming launch of the first study 1.5 months from now (or whenever he can get the money), when do we think the first arm concludes accrual, and when are interim and final results available? That is likely what I will be asked. And I think I just need to bring it up tomorrow morning. We are supposed to discuss his approach to Kessler more generally then.

From: Adam, Stacey (FNIH) [T] (b) (6)
Sent: Tuesday, February 9, 2021 6:43 PM
To: Wholley, David (FNIH) [T (b) (6) Freire, Maria (FNIH) [T] < (b) (6)
Subject: RE: ACTIV-6 Budget Estimate

Hi David,

Do we think this timeline is sufficient?
DCC/CCC Budget

Milestone	Duration (months)
Planning	1.5
Enrollment/Follow-up	20.5
Study Close/Reporting	2.0
Estimated Total Timeline	**24.0**

If so, I should have enough on information to put together the request below. Do we know by when this is needed? AKA when the meeting with Kessler is?

Thanks,
Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: (b) (6) Mobile: (b) (6)

From: Wholley, David (FNIH) [T] (b) (6)
Sent: Tuesday, February 9, 2021 11:36 AM
To: Adam, Stacey (FNIH) [T] (b) (6) Freire, Maria (FNIH) [T] (b) (6)
Subject: RE: ACTIV-6 Budget Estimate

I agree with Stacey ACTIV is us, and this is what we supported for ACTIV 1-3 as I recall. Stacey, I would say that Sarah or someone from NIAID could assist in this. I think the main thing in terms of timeline will be study set up, but if you can give a rough guesstimate of how long the trial would run, that would be indicative of how long the money will be needed. I don't think this can be too specific, given it depends on the number of drugs and when they come in.

From: Adam, Stacey (FNIH) [T] (b) (6)
Sent: Tuesday, February 9, 2021 10:58 AM
To: Freire, Maria (FNIH) [T] < (b) (6) Wholley, David (FNIH) [T] < (b) (6)
Subject: RE: ACTIV-6 Budget Estimate

Hi Maria,

I think it is us. I have a protocol synopsis, which I would just need to shorten a bit. I have the budget. The one piece I don't have is the timeline. I requested this from PCORnet (DCRI/Vanderbilt) yesterday, but they needed a day to discuss and get back to me. I assume this is timeline for stand up of the study correct? Or does it need to include conduct as well?

Thanks,
Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: (b) (6) | Mobile: (b) (6)

From: Freire, Maria (FNIH) [T] < (b) (6)
Sent: Tuesday, February 9, 2021 10:25 AM
To: Wholley, David (FNIH) [T] (b) (6) Adam, Stacey (FNIH) [T] (b) (6)
Subject: Fwd: ACTIV-6 Budget Estimate

Is this us - UGH - or NIH?

From: "Collins, Francis (NIH/OD) [E]" (b) (6)
Date: Tuesday, February 9, 2021 at 10:14:47 AM
To: "Wholley, David (FNIH) [T]" < (b) (6) "Freire, Maria (FNIH) [T]" < (b) (6) 'Tabak, Lawrence (NIH/OD) [E]" (b) (6) , "Lane, Cliff (NIH/NIAID) [E]" (b) (6) "Rutter, Joni (NIH/NCATS) [E]" (b) (6) "Anderson, James (NIH/OD) [E]" (b) (6) "Patterson, Amy (NIH/NHLBI) [E]" (b) (6) , "Parker, Ashley (NIH/OD) [E]" (b) (6)
Subject: FW: ACTIV-6 Budget Estimate

Janet is supportive. I'm ready to bring this to Kessler – but I will need a written description of the project (no more than 2 pages, include the timeline) plus the budget. Can that be assembled ASAP?

FC

From: Woodcock, Janet (b) (6)
Sent: Tuesday, February 9, 2021 9:13 AM
To: Collins, Francis (NIH/OD) [E] (b) (6)
Subject: RE: ACTIV-6 Budget Estimate

It is urgent that this get done. I'd pitch to him the small molecule, repurposed, outpatient point. If we get variants, these agents likely would not be affected. Compared to other expenditures this is small, and the treatments are

generally cheap generic drugs. I think the per-patient cost is a bit high for a low touch study, but we want to power fast enrollment. I'm fine with this, as you remember, I suggested we had to get a pragmatic trial up and running. jw

From: Collins, Francis (NIH/OD) [E] (b) (6)
Sent: Tuesday, February 9, 2021 5:55 AM
To: Woodcock, Janet (b) (6)
Subject: FW: ACTIV-6 Budget Estimate

Hi Janet,

Good progress has been made on the design and plans for implementation of ACTIV-6 for outpatient oral therapies for COVID-19. See below for cost estimate. It's quite a bit higher than I expected, but I believe this can be justified by the importance of the work. I can bring this to David Kessler. He will want to know if you and I are both in favor. Does this look OK to you?

Francis

From: Wholley, David (FNIH) [T] (b) (6)
Sent: Monday, February 8, 2021 9:06 PM
To: Collins, Francis (NIH/OD) [E] (b) (6)
Cc: Freire, Maria (FNIH) [T] (b) (6) , Tabak, Lawrence (NIH/OD) [E] < (b) (6) Lane, Cliff (NIH/NIAID) [E] <cl (b) (6) Read, Sarah (NIH/NIAID) [E] (b) (6) Adam, Stacey (FNIH) [T] (b) (6)
Subject: FW: ACTIV-6 Budget Estimate

Francis,
Here s the estimate you asked for. Sarah is good with the numbers—likes the fact that they accomodate inclusion of additional sites from SIREN as needed.
Let us know what you think.

Thanks, David

From: Adam, Stacey (FNIH) [T] (b) (6)
Sent: Monday, February 8, 2021 7:24 PM
To: Wholley, David (FNIH) [T] (b) (6)
Cc: Read, Sarah (NIH/NIAID) [E] < (b) (6)
Subject: ACTIV-6 Budget Estimate

Hi David,

Here s the initial budget estimate for ACTIV-6. The team would like to estimate at ~$150 million.

The assumptions behind this estimate include:

1. ~280 sites = $10,000 site start-up
2. 15,000 patients total = $5,000/patient to sites
3. Assumes 7-8 agents (current potentials still needing approval from agent prioritization comm ttee are ivermectin, metformin, fluvoxamine, colchicine, montelukast)
4. Assumes a partnership with CVS or similar for early recruitment
5. Additional communications funds will need to be added to the Cross ACTIV Communications Contract
6. (b) (4) million to pay for drug and placebo for some of the drugs selected if a company cannot be found to donate.

7 (b)(4) million in contingencies to cover potential additional Data Coordination Center time, project management, and possibly CRO help if needed

Please let us know if you th nk that this reasonable or if you think we have neglected any cost. If you think this looks good, it can be used for the meeting with Kessler.

Sarah, p ease feel free to add in anything that you think I may have forgotten from our meeting with PCORnet and Vanderbilt today.

Thanks,
Stacey

Personnel	(b) (4)
Travel	
Supplies and Materials	
Other Cost	
Drug/Pharmacy Fees	
Site Start Up Payment	
Site Payment	
External Recruitment	
Communications	
Direct Cost	**$ 110,760,000**
F&A	(b) (4)
Contingency	
Tota Cost	**$ 149,912,000**

Stacey J. Adam, PhD
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Direct: (b) (6) , Mobile: (b) (6)
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11400 Rockville Pike. Suite 600. North Bethesda. MD 20852

From: Menetski, Joseph (FNIH) [T] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=5001AF52DC4A427EA3D34F1E072F8CB7-MENETSKIJP]
Sent: 12/30/2020 2:21:02 PM
To: Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]; Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]; Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Austin, Christopher (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=17597cabc42247548e596778304f781f-austinc]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]; Patterson, Amy (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=afad1ca74b3e449d8b4f3191d65bb70f-pattersa]; Lane, Cliff (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]
Subject: RE: Mutation tracking proposal

I believe that Moncef is referring to the Flu Framework driven by the CDC and we have discussed as a framework for identification of new and emerging variants (particularly Step 1 of the plan). There is some ability to do follow up testing in that CDC network that might be used for COVID, but the assays will need to change. This needs to be augmented to accelerate the process.

Also, the CDC effort has no connection with industry agent sponsors, which makes some sense for flu as there are only a few that are developing agents. It is a very different situation with CoV2 where there are many agents in development.

In the second paragraph of the proposal, we added "The coordination and prioritization will be coordinated with CDC efforts and overseen by representatives from all relevant groups in the healthcare ecosystem led by NIH and CDC and facilitated by FN H." to address the CDC effort and leadership.

Does this answer Moncef's question? Also, there many other efforts to analyze the sequence data, but the team feels that CDC needs to be the lead as it is the CDC mission to keep abreast of surveillance in the US.

Joe

From: Anderson, James (NIH/OD) [E] < (b) (6)
Sent: Wednesday, December 30, 2020 8:41 AM
To: Collins, Francis (NIH/OD) [E] < (b) (6) Wholley, David (FNIH) [T] < (b) (6) Freire, Maria (FNIH) [T] < (b) (6) Tabak, Lawrence (NIH/OD) [E] < (b) (6) Austin, Christopher (NIH/NCATS) [E] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6) Patterson, Amy (NIH/NHLBI) [E] < (b) (6) Lane, Cliff (NIH/NIAID) [E] < (b) (6) Menetski, Joseph (FNIH) [T] < (b) (6)
Subject: RE: Mutation tracking proposal

Joe,
You have done a detailed survey of the virus surveillance programs. Is Moncef referring to the CDC or Sanger or other program as the "flu framework".
Jim

From: Collins, Francis (NIH/OD) [E] (b) (6)
Sent: Wednesday, December 30, 2020 8:36 AM
To: Wholley, David (FNIH) [T] (b) (6) >; Freire, Maria (FNIH) [T] (b) (6) Tabak, Lawrence (NIH/OD) [E] (b) (6) Anderson, James (NIH/OD) [E] (b) (6) ; Austin, Christopher (NIH/NCATS) [E] (b) (6) >; Parker, Ashley (NIH/OD) [E] (Patterson, Amy (NIH/NHLBI) [E] < (b) (6) Lane, Cliff (NIH/NIAID) [E] (b) (6)
Subject: FW: Mutation tracking proposal

FYI. Does someone know about the "flu framework" referred to?

From: Slaoui, Moncef (b) (6)
Sent: Wednesday, December 30, 2020 8:25 AM
To: Collins, Francis (NIH/OD) [E] (b) (6)
Cc: Menetski, Joseph (FNIH) [T] (b) (6)
Subject: RE: Mutation tracking proposal

Francis
Thank you
I will meet with the team and come back to you
I am told that a "similar" concept was used for the Flu pandemic surveillance, have you considered using that framework?
With best regards
Moncef

From: Collins, Francis (NIH/OD) [E] (b) (6)
Sent: Tuesday, December 29, 2020 11:00 AM
To: Slaoui, Moncef (b) (6)
Cc: Menetski, Joseph (FNIH) [T] (b) (6)
Subject: RE: Mutation tracking proposal

Hi Moncef,

Thanks for your quick response. The number I mentioned over the phone was for a scaled-down one-year effort, but it's hard to imagine this being a need that goes away after December 2021. The current proposal is rather more ambitious than what we discussed, designed to cover 120 total variants/year for three years. We think that this volume of mutation research studies is entirely justifiable – but a 40 variant/year proposal (more like what we discussed by phone) would be (b) (5) Years 2 and 3 are based on the efforts from year 1, so would also scale with variants (though there are up front costs that make the first year moderately more expensive). I can send a revised proposal for the 40 variants/year scale, if that would be helpful.

CDC is a major contributor to the proposal, and there is a (b) (5) in the first year to enhance their sequencing efforts. CDC will need to be the main driver of the emerging surveillance effort and a contributor to testing. This proposal is meant to augment and accelerate the process across USG and include industry involvement.

Let me know what I can to help with this consideration.

Francis

From: Slaoui, Moncef (b) (6)
Sent: Tuesday, December 29, 2020 9:04 AM
To: Collins, Francis (NIH/OD) [E] < (b) (6)
Subject: RE: Mutation tracking proposal

Hi Francis
Thank you for following up
We will look into this of course. but two points I would like to share
1- (b) (5)

2-

Thank you
Moncef

From: Collins, Francis (NIH/OD) [E] (b) (6)
Sent: Tuesday, December 29, 2020 8:08 AM
To: Slaoui, Moncef (b) (6)
Cc: Menetski, Joseph (FNIH) [T] (b) (6) Anderson, James (NIH/OD) [E] (b) (6) Tabak, Lawrence (NIH/OD) [E] (b) (6) Wholley, David (FNIH) [T] (b) (6) >, Freire, Maria (FNIH) [T] (b) (6) , Cliff (NIH/NIAID) [E] (b) (6) Fauci, Anthony (NIH/NIAID) [E] (b) (6) Erbelding, Emily (NIH/NIAID) [E] < (b) (6) Marston, Hilary (NIH/NIAID) [E] (b) (6) >; Woodcock, Janet (FDA/CDER) (b) (6) >; Hepburn, Matt (HHS/IOS) (b) (6)
Subject: Mutation tracking proposal

Hi Moncef,

As discussed with you briefly by phone last week, the ACTIV Preclinical Working Group has been hard at work shaping a program that would track newly arising mutations in SARS-CoV-2 and gather information quickly about their significance. Up until now, this has been a bit of a scattershot effort, with a lot of work going on in separate public and private organizations, but no agreement for immediate sharing of the data in a publicly accessible database. The recent emergence of variants in the UK and South Africa has added further urgency to this effort, though this ACTIV plan began before those gained wide public attention.

Attached is a five-step proposal about how to organize a much more effective approach, with significant input from industry, NIH, CDC, and FDA. The three-year budget comes (b) (5) In our earlier conversation, you indicated that this issue is a high prior ty for Operation Warp Speed and BARDA. I would appreciate your thoughts about how best to proceed with this request for support.

I'd be glad to d scuss this further by phone if that would be helpful. Joe Menetski of the Foundation for NIH has been the primary curator of the plan, and would also be glad to provide further details about the components of the plan.

Best, Francis

From: Hodes, Richard (NIH/NIA) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=AAAF8902643342969C60FD551F81A159-HODESR]
Sent: 10/21/2020 1:08:18 PM
To: Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]
CC: Adam, Stacey (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dcd875f0679648859e1cf101c0943414-adamsj4]; Melencio, Cheryl (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=279e14fa7428415bb86087d08b628e6f-melencioc]; Bhattacharyya, Partha (NIH/NIA/ERP) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=69b7bc32b31d4a9781f69fa008fa0522-bhattachary]; Nielsen, Lisbeth (NIH/NIA) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=fb1f678e4b61482eba1afc848390a2a3-nielsenli]
Subject: RE: seeking your help on COVID clinical trials

Hi David,
Partha Bhattacharyya should be the direct contact, copying Lis Nielsen as Director of the relevant NIA division, and me.
Thanks
Richard

From: Wholley, David (FNIH) [T] < (b) (6)
Sent: Wednesday, October 21, 2020 9:05 AM
To: Hodes, Richard (N H/NIA) [E] < (b) (6) Collins, Francis (NIH/OD) [E] < (b) (6)
Cc: Adam, Stacey (FNIH) [T] < (b) (6) Melencio, Cheryl (FNIH) [T] < (b) (6)
Subject: RE: seeking your help on COVID clinical trials

Thanks so much, Richard. Stacey Adam, who is managing the master protocols on the FNIH side and I would be the ones to explore this. Please let me know with whom we should interact on your end

Regards, David

From: Hodes, Richard (NIH/NIA) [E] (b) (6)
Sent: Wednesday, October 21, 2020 8:51 AM
To: Collins, Francis (NIH/OD) [E] (b) (6)
Cc: Wholley, David (FNIH) [T] (b) (6)
Subject: RE: seeking your help on COVID clinical trials

Very good. We'll wait to hear from Davidd.

From: Collins, Francis (NIH/OD) [E] (b) (6)
Sent: Wednesday, October 21, 2020 8:43 AM
To: Hodes, Richard (N H/NIA) [E] (b) (6)
Cc: Wholley, David (FNIH) [T] (b) (6)
Subject: RE: seeking your help on COVID clinical trials

Hi Richard,

Thanks for your rapid response, this is great to know about. I'm looping in David Wholley, and wil ask him or other ACTIV staff to reach out and see what options might exist here.

Francis

From: Hodes, Richard (NIH/NIA) [E] (b) (6)
Sent: Wednesday, October 21, 2020 8:29 AM
To: Collins, Francis (NIH/OD) [E] (b) (6)
Subject: FW: seeking your help on COVID clinical trials

Hi Francis,
In response to your request to hear "right away" about potential resources for expanded COVID clinical trials, I share this description of existing NIA-supported large-scale pragmatic trials with potential for leveraging. We would be happy to work with you and FNIH.
Richard

From: Bhattacharyya, Partha (NIH/NIA/ERP) [E] (b) (6)
Sent: Wednesday, October 21, 2020 8:08 AM
To: Hodes, Richard (N H/NIA) [E] (b) (6)
Cc: Nielsen, Lisbeth (NIH/NIA) [E (b) (6) >; Phillips, John (NIH/NIA/ERP) [E] (b) (6) >
Subject: RE: seeking your help on COVID clinical trials

Dear Dr. Hodes:

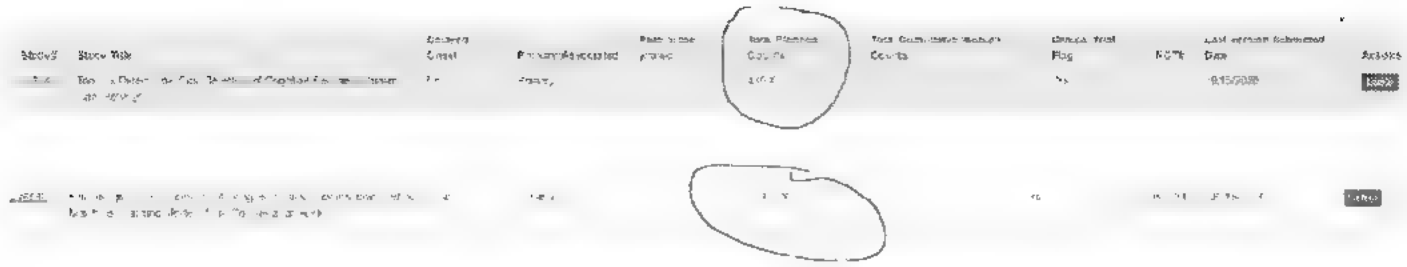
NIA's IMPACT Collaboratory has over 10+ nursing homes chains (with more than 1000 nursing homes) which we can potentially provide trial capacity. The **nursing home staff** can potentially sign-up for trials. I had a discussion in the past with the PI about this specific option. He already suggested this to NIAID's trial network but since it will cost money I think the idea was dropped by NIAID network (they were looking for existing enterprise).

Second option- NIA is currently funding a large pragmatic flu shot trial (N>200K) via Penn Health and Geisinger supported by two Royba. Centers (Penn and NBER). We can reach out to the PI's and explore possibilities and they will "nudge" via text messages and can potentially provide volunteers What I do not know if Penn Health and Geisinger is already part of any COVID network (I attached the presentation). This flu shot trial is using Penn's way to hea th platform which can potentially be used to reach SARS-COV-2 participants.

Third, NIA currently is funding multiple pragmatic clinical trials across the country (appropriate care, prevention, and low cost detection of cognitive decline + Marcel also has few) if we pool them together N across each trial we can reach out to various health systems, including federally designated health centers. The point to note here is we do not have a network as we supported them via RFA but we can ask one the pragmatic trials to play coordinating or network role via a supplement.

Kindly let me know if you need any additional information on second and third option. In order to demonstrate the power of pragmatic trial, I copied and pasted the N or our trials. We just need to support them to coordinate and there is lot of potential.

Thanks
Partha



From: Hodes, Richard (NIH/NIA) [E] (b) (6)
Sent: Wednesday, October 21, 2020 6:51 AM
To: Nielsen, Lisbeth (NIH/NIA) [E] < (b) (6) Hadley, Evan (NIH/NIA) [E] < (b) (6) Masliah, Eliezer (NIH/NIA/ERP) [E] (b) (6) >; Ferrucci, Luigi (NIH/NIA/IRP) [E] (b) (6) Kohanski, Ronald (NIH/NIA) [E] (b) (6) >; Bernard, Marie A. (NIH/NIA) [E] (b) (6) >; Bhattacharyya, Partha (NIH/NIA/ERP) [E] (b) (6) >, Santora, Kenneth (NIH/NIA/ERP) [E] (b) (6)
Subject: FW: seeking your help on COVID clinical trials

Please see Francis' request below. Send directly to me any thoughts that you might have about networks, conventional or pragmatic, that might be appropriate for expanded clinical trials of SARS-CoV-2 therapeutic interventions.
Thank you

From: Collins, Francis (NIH/OD) [E] < (b) (6)
Sent: Wednesday, October 21, 2020 6:13 AM
To: ICDDIR-L@LIST.NIH.GOV
Cc: Wholley, David (FNIH) [T] < (b) (6) Freire, Maria (FNIH) [T] <m (b) (6) Adam, Stacey (FNIH) [T] (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6)
Subject: seeking your help on COVID clinical trials

Dear Colleagues,

As COVID-19 continues to spread across the country, the need to develop additional therapeutic options for those infected with SARS-CoV-2 could hardly be more pressing. The ACTIV partnership of NIH, industry, FDA, and other partners has led much of this large scale effort in the US by prioritizing the most promising therapeutic agents, designing master protocols, and coordinating the various clinical trial networks that can rapidly set up outpatient and inpatient trials. Much progress has been made, but we are still in need of more trial capacity, especially for outpatients. Many US academic centers are already tapped out.

I write to ask if you have any other options to suggest. In particular, trial networks set up to study other conditions, particularly those that utilize community hospitals and outpatient clinics (where most of the COVID-19 patients are), would be of great interest. Repurposing such existing trial networks for COVID-19 has been successfully done in other instances. Resources to support the work would be available almost immediately from Operation Warp Speed, so this should not tap into your budget.

If your IC is aware of such networks and would be willing to discuss this possibility, please contact me right away. David Wholey and his FNIH team can then quickly explore the specifics with you.

Many thanks for your consideration – this is really important.

Francis

From: Collins, Francis (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=410E1CA313F44CED9938E50D2FF0B6C2-COLLINSF]
Sent: 4/27/2020 3:24:47 AM
To: Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Lane, Cliff (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]
CC: Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]
Subject: RE: Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV).

I concur, and it would be great to have that connection before Wednesday.

From: Tabak, Lawrence (NIH/OD) [E] < (b) (6)
Sent: Sunday, April 26, 2020 10:59 PM
To: Collins, Francis (NIH/OD) [E] < (b) (6) Wholley, David (FNIH) [T] < (b) (6) Lane, Cliff (NIH/NIAID) [E] < (b) (6)
Cc: Parker, Ashley (NIH/OD) [E] < (b) (6)
Subject: Re: Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV).

Francis,
Sorry, I thought I had sent note earlier. Both Cliff and Jim indicated we should ask Gen Talley for help but the person we want is Nelson Michael but we need to go through the chain of command. Cliff is willing to arrange this with Gen Talley if you concur,
Larry

From: Francis Collins (b) (6)
Date: Sunday, April 26, 2020 at 10:51 PM
To: "Wholley, David (FNIH) [T]" (b) (6) "Lane, Cliff (NIH/NIAID) [E]" (b) (6) , "Tabak, Lawrence (NIH/OD) [E]" < (b) (6)
Cc: "Parker, Ashley (NIH/OD) [E]" (b) (6)
Subject: RE: Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV).

It seems we are presenting back to back with DOD at the WH on Wednesday. So it would be great to know what became of this effort to connect DOD to ACTIV.

Francis
ing

From: Wholley, David (FNIH) [T] (b) (6)
Sent: Friday, April 24, 2020 3:05 PM
To: Lane, Cliff (NIH/NIAID) [E] (b) (6) >; Tabak, Lawrence (NIH/OD) [E] (b) (6) Collins, Francis (NIH/OD) [E] (b) (6)
Cc: Parker, Ashley (NIH/OD) [E] (b) (6)
Subject: RE: Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV).

Great, thanks. Let me know what is decided—names, which groups they are wanted on—and we will make it happen.

From: Lane, Cliff (NIH/NIAID) [E] (b) (6)
Sent: Friday, April 24, 2020 3:00 PM
To: Tabak, Lawrence (NIH/OD) [E] (b) (6) Wholley, David (FNIH) [T (b) (6) >; Collins, Francis (NIH/OD) [E] (b) (6)
Cc: Parker, Ashley (NIH/OD) [E] < (b) (6)
Subject: Re: Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV).

I know MG Talley. I can give input as well and would be happy to join a call at 3:30. He is the one to approach.

Cliff

From: Lawrence Tabak(>
Date: Friday, April 24, 2020 at 2:57 PM
To: "Wholley, David (FNIH) [T]" (b) (6) , "Collins, Francis (NIH/OD) [E]" (b) (6)
Cc: "Lane, Cliff (NIH/NIAID) [E]" (b) (6) , "Parker, Ashley (NIH/OD) [E]" (b) (6)
Subject: Re: Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV).

I have reached out to Jim Gilman who knows both of these folks. I will speak with him at 3:30 to get his input.
Larry

From: "Wholley, David (FNIH) [T]" < (b) (6)
Date: Friday, April 24, 2020 at 2:27 PM
To: Francis Collins (b) (6) >
Cc: "Lane, Cliff (NIH/NIAID) [E]" (b) (6) >, "Parker, Ashley (NIH/OD) [E]" (b) (6) >, "Tabak, Lawrence (NIH/OD) [E]" < (b) (6)
Subject: FW: Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV).

Hi Francis,
We have been wondering about whether and how to include DoD in ACTIV. John Mascola has reached out with the contacts below Do you know either of them, and do you think they would be a good choice? Or DARPA (which I understand may be under a separate command)? Feel free to reach out, or let us know what else you may need from us. Here's what we (Mike Santos) has pulled together on John's suggestions, in case you don't know them well. Thanks, David

General Michael Talley:

- Commanding General of the US Army Medical Research And Development Command, which oversees
  - U.S. Army Medical Research Institute of Infectious Diseases
    - Does Covid research, has a BSL-4 facility
  - Walter Reed Army Institute of Research
    - Also does Covid research
- General Talley does not appear to have a scientific, medical, technical, or R&D background
- I think he's likely too high-level for this, but may be the right person to start with to get someone from either of his relevant sub-commands, such as the next person

Colonel Deydre Teyhen:

- Commands Walter Reed Army Institute of Research
- Has a PhD in biomechanics and a military career in soldier health and medical readiness
- Has overseen the Army's medical response to Ebola and Zika
- Doesn't appear to have an biopharmaceutical R&D background, but has some relevant context

- Probably an okay but not ideal choice for the ACTIV Leadership Team

Michael Santos, PhD
Associate Vice President, Science | Foundation for the National Institutes of Health

From: Mascola, John (NIH/VRC) [E] < (b) (6)
Sent: Friday, April 24, 2020 1:07 PM
To: Santos, Michae (FNIH) [T] (b) (6)
Cc: Wholley, David (FNIH) [T] (b) (6)
Subject: RE: Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV).

Michael,

Those I know if position of leadership are below.

General Michael Talley (Commander MRDC) (b) (6) .il

https //mrdc amedd.army.mil/index.cfm/about/leadership/cg

COL Deydre Teyhen (Commander, WRAIR) (b) (6)

From: Santos, Michael (FNIH) [T] (b) (6) >
Sent: Friday, April 24, 2020 12:29 PM
To: Mascola, John (NIH/VRC) [E] < (b) (6)
Cc: Wholley, David (FNIH) [T] (b) (6)
Subject: RE: Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV).

John,

Thanks for this suggestion. Do you know specific people in those organizations that you would recommend for addition? We can follow up from there.

Best regards,
Mike

Michael Santos, PhD
Associate Vice President, Science | Foundation for the National Institutes of Health

From: Collins, Francis (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=410E1CA313F44CED9938E50D2FF0B6C2-COLLINSF]
Sent: 4/23/2020 7:04:27 PM
To: Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Lane, Cliff (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]; Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Austin, Christopher (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=17597cabc42247548e596778304f781f-austinc]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]
Subject: FW: [EXTERNAL] Confidential

See second paragraph below, which I will need to answer tomorrow.

-----Original Message-----
From: (b) (6) (b) (6)
Sent: Thursday, April 23, 2020 2:07 PM
To: Collins, Francis (NIH/OD) [E] < (b) (6)
Cc: Stoffels, Paul [JJCUS] < (b) (6)
Subject: Re: [EXTERNAL] Confidential

Francis and Paul
I enjoyed the ACTIV update this week, unfortunately i missed the first part due to a corporate event but the second part was great

As we may discuss ACTIV as an overarching Covid19 Science initiative, pls clarify how the overarching ACTIV steering committee is composed and decision making is performed

Good to know before HEVER

BTW, concerning Covid19, i noted the readout of Remdesivir study in China posted by mistake on WHIO website publicly and was negative or even worsening disease. I assume it will be published in a journal this week. Maybe still a chance it can work moderately if treated earlier but unlikely a game changer as mono therapy . Hard to understand why they did this study w many advanced patients late in disease....

Views ?

(b) (6)

> On Apr 23, 2020, at 10:20 AM, Collins, Francis (NIH/OD) [E] < (b) (6) wrote:
>
> I agree also EMA is a co founder of the ACTIV partnership. They were represented in yesterday's Leadership meeting by Guido Rasi and Marco Cavaleri.
>
> Francis
>
> Sent from my iPhone
>
>> On Apr 23, 2020, at 8:38 AM, (b) (6) wrote:
>>
>> Paul
>> I agree w you that we want a US-EU connectivity
>>
>> Both Hans-Georg and Guido Rasi were invited to HEVER call (b) (6)
>> (b) (6)
>>
>>
>>
>>

>>
>>>> On Apr 23, 2020, at 3:54 AM, Stoffels, Paul [JJCUS] < (b)(6) wrote:
>>>
>>> (b)(6) , Francis,
>>>
>>> Yesterday, I got a call from Hans Georg Eichler, EMA, with the request to appropriately include the European scientific institutions and regulatory authorities in the discussion on new medicine and vaccine development on the industry forums such as Hever and others.
>>> I made a strong point that EMA is a critical agency for Europe and the ROW as it comes to guidance on development as well as regulatory reviews and approval, including working with the WHO and the developing countries on regulatory pathways to accelerate access.
>>> And,
>>> That we will do all effort - as an industry - to include European institutions, as well as European academic and research institution in RD activities.
>>>
>>> Hans Georg will join on Friday in the call. Just wanted to let you know prior to the meeting.
>>>
>>> Thank you
>>>
>>> Paul
>>>
>>>
>>> Verstuurd vanaf mijn iPad

From: Collins, Francis (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=410E1CA313F44CED9938E50D2FF0B6C2-COLLINSF]
Sent: 1/9/2021 12:59:55 AM
To: Menetski, Joseph (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5001af52dc4a427ea3d34f1e072f8cb7-menetskijp]; Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Austin, Christopher (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=17597cabc42247548e596778304f781f-austinc]; Lane, Cliff (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]; Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]; Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]; Patterson, Amy (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=afad1ca74b3e449d8b4f3191d65bb70f-pattersa]
Subject: RE: feedback on activ proposal

Looks good, I'll forward to Anne and see what happens.

Tx, FC

From: Menetski, Joseph (FNIH) [T] < (b) (6)
Sent: Friday, January 8, 2021 7:53 PM
To: Collins, Francis (NIH/OD) [E] < (b) (6) Wholley, David (FNIH) [T] < (b) (6) Freire, Maria (FNIH) [T] < (b) (6) Austin, Christopher (NIH/NCATS) [E] < (b) (6) Lane, Cliff (NIH/NIAID) [E] < (b) (6) Anderson, James (NIH/OD) [E] < (b) (6) Tabak, Lawrence (NIH/OD) [E] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6) Patterson, Amy (NIH/NHLBI) [E] < (b) (6)
Cc: Menetski, Joseph (FNIH) [T] < (b) (6)
Subject: RE: feedback on activ proposal

Dear Francis,

Below please find responses to Dr Schuchat's question 3 and 4 for your review. Please feel free to modify or alter as you wish. If you think these answers miss the mark, please let me know and I will modify the responses.

Best always,
Joe

Questions from Dr Schuchat:

1. The proposal would be improved by greater clarification of how the activities, notably work in BSL3 identified for NCATS, is coordinated with similar efforts currently underway at NIAID-funded laboratories and at CDC laboratories.

NCATS has worked with NIAID to establish HT screening capabilities in the NIAID intramural BSL3 space. NCATS expertise in HTS and assay development and the NCATS drug and chemical libraries will be paired with NIAID virology expertise to

execute standard as well as customized assays. In addition, representatives from CDC and NIAID are actively involved in the coordinat on of the overall testing procedures so that duplication of efforts is eliminated, and the most appropriate facilities are used in a coordinated way.

2. While the current plan seeks to develop an expert group to prioritize work on the variants, we have some concerns that inclusion of academic researchers and industry might be seen as a conflict of interest in determining where USG funding is directed. We feel that it would be more appropriate that an assessment of the availab e data on variants be conducted jointly by USG technical staff at NIAID, FDA, BARDA, and CDC, similar to past PHEMCE activities, to develop routine risk assessment and prioritization reports for HHS and interagency leadership.

What we would propose is scientists from the public and private sector convene to discuss and provide an initial assessment of the var ants, including numerical or narrative information related to how they might be prioritized. This initial assessment would then be shared with government scientists who could then make the actual final decision on priority and d sseminate that final decision through appropriate government channels. This might require convening a group of USG only scientists to have that discussion. With respect to academic scientists, we would have to identify those that would not stand to benefit from the resulting grants and manage any conflicts as is done in the standard academic granting process.

From: Collins, Francis (NIH/OD) [E] < (b) (6)
Sent: Friday, January 8, 2021 8:42 AM
To: Menetski, Joseph (FNIH) [T] (b) (6) ; Wholley, David (FNIH) [T] (b) (6) >; Freire, Maria (FNIH) [T] (b) (6) Austin, Christopher (NIH/NCATS) [E] (b) (6) ; Lane, Cliff (NIH/NIAID) [E] < (b) (6) Anderson, James (NIH/OD) [E] (b) (6) ; Tabak, Lawrence (NIH/OD) [E] (Parker, Ashley (NIH/OD) [E] (Patterson, Amy (NIH/NHLBI) [E] (b) (6)
Subject: FW: feedback on activ proposal

See below for CDC responses to mutation tracking proposal. We will need to respond to items 3 and 4.

FC

From: Schuchat, Anne MD (CDC/OD) < (b) (6)
Sent: Friday, January 8, 2021 8:07 AM
To: Collins, Francis (NIH/OD) [E] (b) (6) >
Cc: Redfield, Robert R (CDC/OD) < (b) (6) Messonnier, Nancy (CDC/DDID/NCIRD/OD) (b) (6) , Walke, Henry (CDC/DDID/NCEZID/DPEI) (b) (6) ; Jernigan, Daniel B. (CDC/DDID/NCIRD/ID) < (b) (6)
Subject: feedback on activ proposal

1. Overall, we think the efforts from ACTIV to support NCBI to develop better tools and databases will be a benefit to the multiple researchers and USG investigators characterizing the variants of SARS-CoV-2.
2. Support for the private sector to increase sequencing results will also benefit the response Notably, supporting commercial laboratories and efforts from sequencing companies will improve overall representativeness and timeliness of information to identify emerging variants.
3. The proposal would be improved by greater clarification of how the activities, notably work in BSL3 identified for NCATS, is coordinated with similar efforts currently underway at NIAID-funded laboratories and at CDC laboratories.
4. While the current plan seeks to develop an expert group to prioritize work on the variants, we have some concerns that inclusion of academic researchers and industry might be seen as a conflict of interest in determining where USG funding is directed. We feel that it would be more appropriate that an assessment of

the availab e data on variants be conducted jointly by USG technical staff at NIAID, FDA, BARDA, and CDC, similar to past PHEMCE activities, to develop routine risk assessment and prioritization reports for HHS and interagency leadership.

Thanks for sharing the proposal with us and we look forward on working together on this critica. effort.

Anne Schuchat, MD
Principal Deputy Director
Centers for Disease Control and Prevention
Rear Admiral, US Public Health Service (b) (6)

From: Mascola, John (NIH/VRC) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7F78B40A596B4CA4A2850A429D1AE3F2-JMASCOLA]
Sent: 12/20/2020 11:28:02 PM
To: Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]; Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Menetski, Joseph (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5001af52dc4a427ea3d34f1e072f8cb7-menetskijp]; Graham, Barney (NIH/VRC) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=171892ff532b4c208a546e6fc7e87b8a-bgraham]
CC: Fauci, Anthony (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=df38103d75134f658ae2d356f0396b94-afauci]; Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Austin, Christopher (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=17597cabc42247548e596778304f781f-austinc]; Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]; Patterson, Amy (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=afad1ca74b3e449d8b4f3191d65bb70f-pattersa]; Lane, Cliff (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]
Subject: RE: N501Y variant in the UK
Attachments: Kemp - UK transmission S-protein variant pdf; Report-1_COG-UK_19-December-2020_SARS-CoV-2-Mutations.pdf

From Barney,

We'll digest and summarize.

From: Mascola, John (NIH/VRC) [E]
Sent: Sunday, December 20, 2020 5:58 PM
To: Collins, Francis (NIH/OD) [E] < (b) (6) Wholley, David (FNIH) [T] < (b) (6) Menetski, Joseph (FNIH) [T] < (b) (6) Graham, Barney (NIH/VRC) [E] < (b) (6)
Cc: Fauci, Anthony (NIH/NIAID) [E] < (b) (6) Freire, Maria (FNIH) [T] < (b) (6) Tabak, Lawrence (NIH/OD) [E] < (b) (6) Austin, Christopher (NIH/NCATS) [E] < (b) (6) Anderson, James (NIH/OD) [E] < (b) (6) Patterson, Amy (NIH/NHLBI) [E] < (b) (6) Lane, Cliff (NIH/NIAID) [E] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6)
Subject: RE: N501Y variant in the UK

Francis,

Is there a primary paper here – other than news reports? I don't see anything posted on bioRxiv.

We are making at testing most of the common variants including D614G, M439K and others. They can be made as Env pseudoviruses in BSL2 and tested vs vaccine sera.

For now, we can model 501Y onto the structure – and see exactly where it is, while we make the variant.
In vivo transmissibility and pathogenicity data would take longer – but perhaps some in UK have done this.

New variants will continue to occur – so without a specific reason for concern, we should take them in stride and track and study them as you suggest.

John

From: Collins, Francis (NIH/OD) [E] (b) (6)
Sent: Sunday, December 20, 2020 4:06 PM
To: Wholley, David (FNIH) [T] (b) (6) Menetski, Joseph (FNIH) [T] (b) (6) >; Graham, Barney (NIH/VRC) [E] < (b) (6) . Mascola, John (NIH/VRC) [E] < (b) (6)
Cc: Fauci, Anthony (NIH/NIAID) [E] (b) (6) >; Freire, Maria (FNIH) [T] (b) (6) ; Tabak, Lawrence (NIH/OD) [E] (b) (6) ; Austin, Christopher (NIH/NCATS) [E] < (b) (6) Anderson, James (NIH/OD) [E] (b) (6) Patterson, Amy (NIH/NHLBI) [E] (b) (6) Lane, Cliff (NIH/NIAID) [E] (b) (6) >; Parker, Ashley (NIH/OD) [E] < (b) (6)
Subject: N501Y var ant in the UK

Hi David, Joe, Barney, and John,

The N501Y variant in the spike protein has risen rapidly in frequency in the UK and is causing much alarm there about increased transmissibility, now causing 62% of cases in London. See https //www.wsj com/articles/what-we-know-about-the-new-covid-19-strain-in england-11608423416 Has the ACTIV mutation tracking team already jumped on this to see what its effects on vaccines and mAbs might be? Have the VRC experts already done an assessment of this one?

Francis

From: Austin, Christopher (NIH/NCATS) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=17597CABC42247548E596778304F781F-AUSTINC]
Sent: 12/20/2020 9:36:47 PM
To: Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]; Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Lane, Cliff (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]; Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]; Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]; Patterson, Amy (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=afad1ca74b3e449d8b4f3191d65bb70f-pattersa]
Subject: RE: Need a small favor... pass onto Dr. Fauci? *NEW* incredible data on FLV (submitted to JAMA today)

Yes indeed, why have not brought this to the war room before, but rather have handled The good news is that the PI actually doing the trials – Eric Lenze from WashU – is very good, well known to us and NIMH, and methodical rather than emotional.

From: Collins, Francis (NIH/OD) [E] < (b) (6)
Sent: Sunday, December 20, 2020 4:26 PM
To: Austin, Christopher (NIH/NCATS) [E] < (b) (6) Tabak, Lawrence (NIH/OD) [E] < (b) (6) Lane, Cliff (NIH/NIAID) [E] < (b) (6) Wholley, David (FNIH) [T] < (b) (6) Freire, Maria (FNIH) [T] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6) Anderson, James (NIH/OD) [E] < (b) (6) Patterson, Amy (NIH/NHLBI) [E] < (b) (6)
Subject: RE: Need a small favor... pass onto Dr. Fauci? *NEW* incredible data on FLV (submitted to JAMA today)

Let's discuss at War Room tomorrow. I have to say that Mr. Kirsch's rather emotional approach to this situation does not inspire confidence – but if there's a way for us to help the WashU trial to enroll, let's see about that.

FC

From: Austin, Christopher (NIH/NCATS) [E] (b) (6)
Sent: Sunday, December 20, 2020 1:33 PM
To: Collins, Francis (NIH/OD) [E] (b) (6) >, Tabak, Lawrence (NIH/OD) [E] < (b) (6) Lane, Cliff (NIH/NIAID) [E] (b) (6) Wholley, David (FNIH) [T] (b) (6) Freire, Maria (FNIH) [T] (b) (6) >; Parker, Ashley (NIH/OD) [E] < (b) (6) Anderson, James (NIH/OD) [E] (b) (6) >; Patterson, Amy (NIH/NHLBI) [E] (b) (6)
Subject: FW: Need a small favor... pass onto Dr. Fauci? *NEW* incredible data on FLV (submitted to JAMA today)

Francis,

Wanted to make you aware of this discussion in case you get asked about it. This a long email thread, but the first four entries below will give you the current status. The manuscript enclosed was not accepted by JAMA but has now been submitted to Open Forum Infectious Diseases.

Steve Kirsch https://en.wikipedia.org/wiki/Steve_Kirsch is a well-connected tech entrepreneur who has been funding and advocating for COVID efforts.

Additional action we might consider at this point is helping w outpatient recruitment, including potentially via the CVS connection, since Eric Lenze (WashU PI who is running the larger confirmatory trial) is having difficulty. NCATS is helping w logistics via the CTSAs at WashU and Utah.

We can discuss War Room tomorrow if you wish.

Chris

From: Steve Kirsch < (b) (6)
Sent: Sunday, December 20, 2020 12:42 AM
To: Austin, Christopher (NIH/NCATS) [E] <au (b) (6)
Cc: Woodcock, Janet (FDA/CDER) (b) (6)
Subject: RE: Need a small favor... pass onto Dr. Fauci? *NEW* incredible data on FLV (submitted to JAMA today)

I was warned that Dr Fauci would immediately dismiss it as not enough data. Sure the numbers are small, but NONE of these people had anywhere close to ANY respiratory (or other) issues. So **larger numbers will not change the outcome at all.** So all we are doing by not taking action is simply wasting time. With larger numbers, we'll be able to find out that it is 99.7 effective vs. 99.8% effective. THAT'S AN INSANE WASTE OF LIVES.

the death rate is now at a new high... one death every 24 seconds. The death rate can be slashed to near zero if Dr. Fauci can be convinced this is on the level.

I have suggested a viable way to cut the death rate to near zero using this cheap generic drug.

It is supported 250% by the Dean of the Medical School at Emory who is NOW basically putting his entire medical career on the line by coming out and supporting this publicly and calling for it being the standard of care. He s not crazy. He's one of the most cited scientists on the planet. The data is super compelling. EVEN his biggest detractors, when he asked, "OK, so what would *you* take if *you* got COVID ?"refused to answer him! They couldn't admit he was right. Silence!

At Emory, they had every ID doc look at it and they had NO CRITICISMS of the data. They were basically just chicken to take a stand. Reputational risk. Yet the p-value is .0001 for just 2 studies. The reputational risk is on NOT ACTING on this. It's immoral. They are refusing to act on the evidence in plain sight that could save lives.

I have only one question. What will it take to get Dr. Fauci to take a 10 minute call from Dean Sukhatme so we can address his concerns?

steve

From: Read, Sarah (NIH/NIAID) [E] (b) (6)
Sent: Saturday, December 19, 2020 10:27 PM
To: Austin, Christopher (NIH/NCATS) [E] (b) (6) >; Adam, Stacey (FNIH) [T] (b) (6) >; Lane, Cliff (NIH/NIAID) [E] < (b) (6)

Cc: Woodcock, Janet (FDA/CDER) (b) (6)
Subject: RE: Need a small favor... pass onto Dr. Fauci? *NEW* incredible data on FLV (submitted to JAMA today)

Hi Chris,
Thanks for the information. The agent prioritization committee did recommend fluvoxamine to ACTIV-2, however the ACTIV2 team decided not to proceed given the phase III that Eric Lenze is implementing. That said, they are open to incorporating it if Eric's trial is not able to recruit.

I can also share this information with the program staff who are assigned to Eric's grant application.

Sarah

From: Austin, Christopher (NIH/NCATS) [E] < (b) (6)
Sent: Saturday, December 19, 2020 5:19 PM
To: Read, Sarah (NIH/NIAID) [E] (b) (6) Adam, Stacey (FNIH) [T] (b) (6) ; Lane, Cliff (NIH/NIAID) [E] < (b) (6)
Cc: Woodcock, Janet (FDA/CDER) < (b) (6)
Subject: FW: Need a small favor... pass onto Dr. Fauci? *NEW* incredible data on FLV (submitted to JAMA today)

Sara, Stacey, and Cliff,

I am forwarding this information so you are aware and Tony can be made aware also, in case he gets asked about it. The letter enclosed has not been published; it was not accepted by JAMA.

Eric Lenze, the PI of the study referred to in the letter https://jamanetwork.com/journals/jama/fullarticle/2773108, is now conducting a larger trial (800 people), at this point funded by philanthropy; he has submitted a grant application to NIAID for funding that will apparently be reviewed in January and will be necessary for Dr. Lenze to complete the trial.

Janet is aware and following. Stacey has told me that ACTIV has been following this drug and decided not to put it into an ACTIV trial since Dr. Lenze already has a trial started. NCATS is assisting with logistics of the trial via the WashU CTSA hub, but does not have funding or a mechanism to support the trial itself.

Please let me know if you decide to do anything on fluvoxamine. The preliminary data do look promising.

Thanks,

Chris

From: Austin, Christopher (NIH/NCATS) [E]
Sent: Saturday, December 19, 2020 5:06 PM
To: Steve Kirsch < (b) (6)
Cc: David Seftel (b) (6) Woodcock, Janet (FDA/CDER) (b) (6)
Subject: RE. Need a small favor... pass onto Dr. Fauci? *NEW* incredible data on FLV (submitted to JAMA today)

Steve, thank you. I am actively talking to Dr. Lenze. And Dr. Fauci is now aware of the data on fluvoxamine.

From: Steve Kirsch (b) (6)
Sent: Friday, December 18, 2020 10:32 PM
To: Austin, Christopher (NIH/NCATS) [E] < (b) (6)
Cc: David Seftel <d (b) (6) Woodcock, Janet (FDA/CDER) < (b) (6)
Subject: RE: Need a small favor... pass onto Dr. Fauci? *NEW* incredible data on FLV (submitted to JAMA today)

if we can get 10 minutes with Dr. Fauci it would be transformative. I saw him on CNN just now bemoaning the fact that the vaccine wasn't tested in a population proportioned by those most affected. In our case, we field tested fluvoxamine with a population that is 84% latino who have a hospitalization rate of 12.5% and it was 100% protective. I have been warned that "you'll never convince him with N=265 (combined) and p values of .009 and .005, but the fact is that every single patient never got anywhere close to any respiratory decline. He needs to hear this directly from the NIH-funded researcher who did the study. That researcher thinks it is crazy that people aren't jumping on this. And they would be jumping if HCQ hadn't poisoned the well. Let's not compound the HCQ mistake by ignoring FLV. It's not right. this is a solution to the 1 person/min who dies today despite a vaccine. With Dr. Fauci's help we can save most if not all of those people.

From: Steve Kirsch < (b) (6)
Sent: Friday, December 18, 2020 3:53 PM
To: Austin, Christopher (NIH/NCATS) [E] < (b) (6)
Cc: David Seftel (b) (6) Woodcock, Janet (FDA/CDER) (b) (6)
Subject: RE: Need a small favor... pass onto Dr. Fauci? *NEW* incredible data on FLV (submitted to JAMA today)

JAMA rejected it per their policy of not accepting ANY covid-related letters. so we are exploring other options including self-publishing it.

The enrollment rate of the Phase 3 study is currently at 0 per day. So it is going nowhere very slowly We have very little money to promote. BARDA has no money and the small number of wealthy philanthropists who care about this approach have been tapped.

The Biden COVID committee was alerted about FLV, but they didn't contact us to talk to the physicians running either study. They just hit delete, even though it was forwarded to them by Secretary Vilsack.

I was banned for life by Medium for suggesting that FLV was 100% effective in clinical studies done to date. My friends have had their posts removed. JAMA won't consider the follow on letter per their policy. Facebook won't run the IRB approved ads for the study. Emory just turned down a request by their Dean of the School of Medicine to make FLV standard of care... they had NO CRITICISMS at all of the data They just didn't want to risk their reputation on something nobody else is talking about.

This is why mentions by Dr. Fauci are so critical. If we can get 10 minutes of his time, I'm sure we can convince him this is way better than placebo. The placebo is known to put people in the hospital and morgue. There is no ev dence that FLV is does either.

We KNOW what the short and long term effects are. Angela did preliminary analysis of the long term data in the N=152 RCT and placebo and FLV looked similar.

But short term in EVERY study we are aware of, Sigma 1 activation shows benefit. We have the obs study in France.. they didn't even know about sigma1, yet the effectiveness was ordered by sigma1 activation of the SSRI's tested. with only one excewption, the greater the sigma1, the greater the protection. So we have two trials in a row, both showing 100% protection, the last one showing 12.5% hospitalization for placebo.

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So two questions:

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Sent: Friday, December 18, 2020 11:55 AM
To: Steve Kirsch (b) (6)
Cc: David Seftel (b) (6) >; Woodcock, Janet (FDA/CDER) (b) (6)
Subject: RE: Need a small favor... pass onto Dr. Fauci? *NEW* incredible data on FLV (submitted to JAMA today)

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I appreciate your efforts and please be assured that the trans-agency coordination teams are looking at these data very seriously.

Best,

Chris

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Importance: High

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Howard Bauchner is supportive of FLV, but he won't say anything.

NOT SAYING ANYTHING IS KEEPING THIS DATA FROM THE WORLD and it doing a huge disservice to America.

We lose 1 person every minute. If this information were known, we could eliminate virtually all those deaths.

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I promise we will knock his socks off... this drug was able to REVERSE respiratory distress in every case, at all stages of the disease

And it does so without any noticeable side effects. The doctor at GG Fields called the results the most extraordinary effect he's ever seen in his medical career.

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Thanks Chris.

-steve

From: Tabak, Lawrence (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=02E2283685FF4E9988E3770CFC7EE770-TABAKL]
Sent: 12/20/2020 7:15:03 PM
To: Austin, Christopher (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=17597cabc42247548e596778304f781f-austinc]
CC: Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]; Lane, Cliff (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]; Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]; Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]; Patterson, Amy (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=afad1ca74b3e449d8b4f3191d65bb70f-pattersa]
Subject: Re: Need a small favor... pass onto Dr. Fauci? *NEW* incredible data on FLV (submitted to JAMA today)

thanks

From: "Austin, Christopher (NIH/NCATS) [E]" < (b) (6)
Date: Sunday, December 20, 2020 at 2:08 PM
To: "Tabak, Lawrence (NIH/OD) [E]" < (b) (6)
Cc: Francis Coll ns < (b) (6) "Lane, Cliff (NIH/NIAID) [E]" < (b) (6) "Wholley, David (FNIH) [T]" <dwholley@fnih.org>, "Freire, Maria (FNIH) [T]" < (b) (6) "Parker, Ashley (NIH/OD) [E]" < (b) (6) "Anderson, James (NIH/OD) [E]" < (b) (6) "Patterson, Amy (NIH/NHLBI) [E]" < (b) (6)
Subject: RE: Need a small favor... pass onto Dr. Fauci? *NEW* incredible data on FLV (submitted to JAMA today)

Sorry, try this one

From: Tabak, Lawrence (NIH/OD) [E] < (b) (6)
Sent: Sunday, December 20, 2020 2:03 PM
To: Austin, Christopher (NIH/NCATS) [E] < (b) (6)
Subject: Re: Need a small favor... pass onto Dr. Fauci? *NEW* incredible data on FLV (submitted to JAMA today)

File was damaged – I am unable to open

From: "Austin, Christopher (NIH/NCATS) [E]" <a (b) (6)
Date: Sunday, December 20, 2020 at 1:32 PM
To: Francis Collins (b) (6) >, "Tabak, Lawrence (NIH/OD) [E]' (b) (6) . "Lane, Cliff (NIH/NIAID) [E]" < (b) (6) "Wholley, David (FNIH) [T]" < (b) (6) "Freire, Maria (FNIH) [T]" < (b) (6) "Parker, Ashley (NIH/OD) [E]" (b) (6) . "Anderson, James (NIH/OD) [E]" (b) (6) , "Patterson, Amy (NIH/NHLBI) [E]" < (b) (6)
Subject: FW: Need a small favor... pass onto Dr. Fauci? *NEW* incredible data on FLV (submitted to JAMA today)

Francis,

Wanted to make you aware of this discussion in case you get asked about it. This a long email thread, but the first four entries below will give you the current status. The manuscript enclosed was not accepted by JAMA but has now been submitted to Open Forum Infectious Diseases.

Steve Kirsch https://en.wikipedia.org/wiki/Steve_Kirsch is a well-connected tech entrepreneur who has been funding and advocating for COVID efforts.

Addit onal action we might consider at this point is helping w outpatient recruitment, including potentially via the CVS connection, since Eric Lenze (WashU PI who is running the larger confirmatory trial) is having difficulty. NCATS is helping w logistics via the CTSAs at WashU and Utah.

We can discuss War Room tomorrow if you wish.

Chris

From: Steve Kirsch (b) (6)
Sent: Sunday, December 20, 2020 12:42 AM
To: Austin, Christopher (NIH/NCATS) [E] (b) (6)
Cc: Woodcock, Janet (FDA/CDER) (b) (6)
Subject: RE: Need a small favor... pass onto Dr. Fauci? *NEW* incredible data on FLV (submitted to JAMA today)

I was warned that Dr. Fauci would immediately dismiss it as not enough data. Sure the numbers are small, but NONE of these people had anywhere close to ANY respiratory (or other) issues. So **larger numbers will not change the outcome at all.** So all we are doing by not taking action is simply wasting time. With larger numbers, we'll be able to find out that it is 99.7 effective vs. 99.8% effective. THAT'S AN INSANE WASTE OF LIVES.

the death rate is now at a new high... one death every 24 seconds. The death rate can be slashed to near zero if Dr. Fauci can be convinced this is on the level.

I have suggested a viable way to cut the death rate to near zero using this cheap generic drug.

It is supported 250% by the Dean of the Medical School at Emory who is NOW basically putting his entire medical career on the line by coming out and supporting this publicly and calling for it being the standard of care. He's not crazy. He's one of the most cited scientists on the planet. The data is super compelling. EVEN his biggest detractors, when he asked, "OK, so what would *you* take if *you* got COVID ?"refused to answer him! They couldn't admit he was right. Silence!

At Emory, they had every ID doc look at it and they had NO CRITICISMS of the data. They were basically just chicken to take a stand. Reputational risk. Yet the p-value is .0001 for just 2 studies. The reputational risk is on NOT ACTING on this. It's immoral. They are refusing to act on the evidence in plain sight that could save lives.

I have only one question What will it take to get Dr. Fauci to take a 10 minute call from Dean Sukhatme so we can address his concerns?

-steve

From: Read, Sarah (NIH/NIAID) [E] < (b) (6)
Sent: Saturday, December 19, 2020 10:27 PM

To: Austin, Christopher (NIH/NCATS) [E] < (b) (6) Adam, Stacey (FNIH) [T] < (b) (6) Lane, Cliff (NIH/NIAID) [E] < (b) (6)
Cc: Woodcock, Janet (FDA/CDER) (b) (6)
Subject: RE: Need a small favor... pass onto Dr. Fauci? *NEW* incredible data on FLV (submitted to JAMA today)

Hi Chris,
Thanks for the information. The agent prioritization committee did recommend fluvoxamine to ACTIV-2, however the ACTIV2 team decided not to proceed given the phase III that Eric Lenze is implementing. That said, they are open to incorporating it if Eric's trial is not able to recruit.

I can also share this information with the program staff who are assigned to Eric's grant application.

Sarah

From: Austin, Christopher (NIH/NCATS) [E] (b) (6)
Sent: Saturday, December 19, 2020 5:19 PM
To: Read, Sarah (NIH/NIAID) [E] < (b) (6) Adam, Stacey (FNIH) [T] (b) (6) ; Lane, Cliff (NIH/NIAID) [E] (b) (6)
Cc: Woodcock, Janet (FDA/CDER) (b) (6)
Subject: FW: Need a small favor. . pass onto Dr. Fauci? *NEW* incredible data on FLV (submitted to JAMA today)

Sara, Stacey, and Cliff,

I am forwarding this information so you are aware and Tony can be made aware also, in case he gets asked about it. The letter enclosed has not been published; it was not accepted by JAMA.

Eric Lenze, the PI of the study referred to in the letter https //jamanetwork com/journals/jama/ful article/2773108, is now conducting a larger trial (800 people), at this point funded by philanthropy; he has submitted a grant application to NIAID for funding that will apparently be reviewed in January and will be necessary for Dr. Lenze to complete the trial.

Janet is aware and following. Stacey has told me that ACTIV has been following this drug and decided not to put it into an ACTIV trial since Dr. Lenze already has a trial started. NCATS is assisting with logistics of the trial via the WashU CTSA hub, but does not have funding or a mechanism to support the trial itself.

Please let me know if you decide to do anything on fluvoxamine. The preliminary data do look promising.

Thanks,

Chris

From: Austin, Christopher (NIH/NCATS) [E]
Sent: Saturday, December 19, 2020 5:06 PM
To: Steve Kirsch (b) (6) >
Cc: David Seftel (b) (6) >; Woodcock, Janet (FDA/CDER) (b) (6)
Subject: RE: Need a small favor... pass onto Dr. Fauci? *NEW* incredible data on FLV (submitted to JAMA today)

Steve, thank you. I am actively talking to Dr. Lenze. And Dr. Fauci is now aware of the data on fluvoxamine.

From: Steve Kirsch (b) (6)
Sent: Friday, December 18, 2020 10:32 PM
To: Austin, Christopher (NIH/NCATS) [E] (b) (6)

Cc: David Seftel < (b) (6) Woodcock, Janet (FDA/CDER) (b) (6)
Subject: RE: Need a small favor... pass onto Dr. Fauci? *NEW* incredible data on FLV (submitted to JAMA today)

If we can get 10 minutes with Dr. Fauci it would be transformative. I saw him on CNN just now bemoaning the fact that the vaccine wasn't tested in a population proportioned by those most affected. In our case, we field tested fluvoxamine with a population that is 84% latino who have a hospitalization rate of 12.5% and it was 100% protective. I have been warned that "you'll never convince him with N=265 (combined) and p values of .009 and .005, but the fact is that every single patient never got anywhere close to any respiratory decline. He needs to hear this directly from the NIH-funded researcher who did the study. That researcher thinks it is crazy that people aren't jumping on this. And they would be jumping if HCQ hadn't poisoned the well. Let's not compound the HCQ mistake by ignoring FLV. It's not right. this is a solution to the 1 person/min who dies today despite a vaccine. With Dr. Fauci's help we can save most if not all of those people.

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To: Austin, Christopher (NIH/NCATS) [E] < (b) (6)
Cc: David Seftel (b) (6) ; Woodcock, Janet (FDA/CDER) < (b) (6)
Subject: RE: Need a small favor... pass onto Dr. Fauci? *NEW* incredible data on FLV (submitted to JAMA today)

JAMA rejected it per their policy of not accepting ANY covid-related letters. so we are exploring other options including self-publishing it.

The enrollment rate of the Phase 3 study is currently at 0 per day. So it is going nowhere very slowly. We have very little money to promote. BARDA has no money and the small number of wealthy philanthropists who care about this approach have been tapped.

The Biden COVID committee was alerted about FLV, but they didn't contact us to talk to the physicians running either study. They just hit delete, even though it was forwarded to them by Secretary Vilsack.

I was banned for life by Medium for suggesting that FLV was 100% effective in clinical studies done to date My friends have had their posts removed. JAMA won't consider the follow on letter per their policy. Facebook won't run the IRB approved ads for the study. Emory just turned down a request by their Dean of the School of Medicine to make FLV standard of care... they had NO CRITICISMS at all of the data. They just didn't want to risk their reputation on something nobody else is talking about.

This is why mentions by Dr. Fauci are so critical. If we can get 10 minutes of his time, I'm sure we can convince him this is way better than placebo. The placebo is known to put people in the hospital and morgue. There is no ev dence that FLV is does either.

We KNOW what the short and long term effects are Angela did preliminary analysis of the long term data in the N=152 RCT and placebo and FLV looked similar.

But short term in EVERY study we are aware of, Sigma 1 activation shows benefit. We have the obs study in France... they didn't even know about sigma1, yet the effectiveness was ordered by sigma1 activation of the SSRI's tested. with only one excewption, the greater the sigma1, the greater the protection. So we have two trials in a row, both showing 100% protection, the last one showing 12.5% hospitalization for placebo.

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So two questions:

1. Do you think this will be successful?
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Sent: 12/21/2020 9:29:25 PM
To: Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]; Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Austin, Christopher (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=17597cabc42247548e596778304f781f-austinc]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]; Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]; Patterson, Amy (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=afad1ca74b3e449d8b4f3191d65bb70f-pattersa]; Menetski, Joseph (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5001af52dc4a427ea3d34f1e072f8cb7-menetskijp]
Subject: Confidential - NIAID Follow-up on transmission study

In a closed meeting this morning, NIAID leadership discussed the transmission study with ad hoc input from Doug Lowy representing the ACTIV vaccine group. All recognized the elegance of the design and the importance of the question. However, there was little enthusiasm for the study as presented due to feeling it is operationally challenging and in need of rapid implementation There was discussion of trying to look at other ways of informing the question of transmission – one possibility being through the logical, albeit unvalidated, surrogate of nasopharyngeal viral titer and asymptomatic infection in vaccinees vs. placebo groups.

Cliff

From: Lane, Cliff (NIH/NIAID) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=2D7E368A3137473BBCE161547A82F2DE-CLANE]
Sent: 1/8/2021 6:36:32 PM
To: Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]; Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Austin, Christopher (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=17597cabc42247548e596778304f781f-austinc]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]; Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]; Patterson, Amy (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=afad1ca74b3e449d8b4f3191d65bb70f-pattersa]
Subject: Re: Follow-up on Correlates of Immunity and on PPD and ACTIV-2

Yes, please share in any way that you think appropriate

Cliff

From: "Wholley, David (FNIH) [T]" < (b) (6)
Date: Friday, January 8, 2021 at 1:34 PM
To: "Lane, Cliff (NIH/NIAID) [E]" < (b) (6) "Collins, Francis (NIH/OD) [E]" < (b) (6) Lawrence Tabak < (b) (6) "Freire, Maria (FNIH) [T]" < (b) (6) "Austin, Christopher (NIH/NCATS) [E]" < (b) (6) "Parker, Ashley (NIH/OD) [E]" < (b) (6) "Anderson, James (NIH/OD) [E]" < (b) (6) "Patterson, Amy (NIH/NHLBI) [E]" < (b) (6)
Subject: RE: Follow-up on Correlates of Immunity and on PPD and ACTIV-2

Cliff is it OK to share this with Doug Lowy and Mike Santos? I believe discussion of this topic will fall under Doug's Working Group section on next Thursday's Leadership Team call. Also, if there are further questions about the plan, would Doug or Mike approach you to get them answered? Want to make sure what is said is consistent with NIAID/NIH leadership. Thanks

From: Lane, Cliff (NIH/NIAID) [E] < (b) (6)
Sent: Friday, January 8, 2021 12:25 PM
To: Collins, Francis (NIH/OD) [E] < (b) (6) Tabak, Lawrence (NIH/OD) [E] < (b) (6) Freire, Maria (FNIH) [T] < (b) (6) Austin, Christopher (NIH/NCATS) [E] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6) Anderson, James (NIH/OD) [E] < (b) (6) Patterson, Amy (NIH/NHLBI) [E] < (b) (6) Wholley, David (FNIH) [T] < (b) (6)
Subject: Follow-up on Correlates of Immunity and on PPD and ACTIV-2

The NIAID VRC (Rick Koup) and U. Washington (Larry Corey) are getting samples to study correlates of immunity from the Moderna, JNJ, and the other OWS supported trials as a term of the contracts. Pfizer has declined to participate as part of the group – preferring to do things on their own. Given the limited number of cases in the vaccine recipients and likely limited amount of stored samples this is unfortunate and perhaps worth mentioning on an ACTIV leadership call.

Below is my email exchange with Peter Kim regarding PPD and ACTIV-2.
Looks like Peter would benefit from more specific information regarding the potential NIGMS sites.

Cliff

Cliff, thanks for this note. In general, pace of site activation continues to be an issue for all eligible sites. We have found that it's a complex issue that certainly involves PPD but also goes beyond PPD (e.g. when we pressed PPD to communicate more frequently with sites to accelerate site activation, we started getting complaints from sites that they could not move any faster, we also found that some sites were activated without all the necessary requirements in place).

Having said this, I had not heard specifically about issues with NIGMS sites, but I will look into it. Certainly if there are sites that feel that things are not moving fast enough for them, we can push PPD to move faster.

Thanks,

Peter

From: Lane, Cliff (NIH/NIAID) [E(
Sent: Friday, January 8, 2021 10:12 AM
To: Kim, Peter (NIH/NIAID) [E] (b) (6)
Cc: Read, Sarah (NIH/NIAID) [E] < (b) (6) Dieffenbach, Carl (NIH/NIAID) [E] (b) (6)
Subject: Question from Dr. Collins

Peter,

On an ACTIV call this morning it was noted that PPD has not been as responsive as you would like them to be regarding support of ACTIV-2; particularly with respect to adding sites from the NIGMS network to ACTIV-2.

Is this accurate and, if so, are there things that can be done (within NIAID, within NIH) to be of help?

+Sarah and Carl for awareness.

Thanks,

Cliff

From: Wholley, David (FNIH) [T] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=CD9E702FCF28414883D0B6996D677257-WHOLLEYD]
Sent: 1/22/2021 7:00:51 PM
To: Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]
CC: Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Lane, Cliff (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]; Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Austin, Christopher (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=17597cabc42247548e596778304f781f-austinc]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]; Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]; Patterson, Amy (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=afad1ca74b3e449d8b4f3191d65bb70f-pattersa]; Adam, Stacey (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dcd875f0679648859e1cf101c0943414-adamsj4]
Subject: Update on Pfizer Antiviral Agent (PF-07304814)

Hi Francis,

Following up on your question from this morning's war room regarding Pfizer's recent submission of their ant viral agent, the ACTIV agent prioritization group met this morning and the reviews were very favorable toward the agent overall. The reviewers' remaining questions were focused primarily on the need for more clinical data (since the compound is still in Phase 1), and whether the agent has been tested with remdesivir.

The FNIH/Deloitte team are following up with Pfizer to ask these questions and to understand their current plans for studies beyond Phase 1. In fact, Stacey Adam is reaching out directly to Leisa at Pfizer and the team ahead of the normally scheduled outreach to let them know the outcome of the review and try to expedite getting the additional information from them if they have it. In the meantime, the reviewers thought that it would be worthwhile to share their evaluation of the agent with ACTIV 3 and John Beigel (to assess its fit for ACTT or ACTIV 5), so we will be helping to coordinate those discussions.

Thanks, David

From: Tabak, Lawrence (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=02E22836B5FF4E9988E3770CFC7EE770-TABAKL]
Sent: 1/31/2021 1:48:00 PM
To: Rutter, Joni (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=157b2517ddb546a8a72844c35eadb062-jrutter]; Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]; Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]; Lane, Cliff (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]; Patterson, Amy (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=afad1ca74b3e449d8b4f3191d65bb70f-pattersa]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]
Subject: Re: Input requested on STORM

Will do
Thanks
Larry

From: "Rutter, Joni (NIH/NCATS) [E]" < (b) (6)
Date: Sunday, January 31, 2021 at 8:46 AM
To: "Tabak, Lawrence (NIH/OD) [E]" < (b) (6) Francis Collins < (b) (6) "Freire, Maria (FNIH) [T]" < (b) (6) "Wholley, David (FNIH) [T]" < (b) (6) "Anderson, James (NIH/OD) [E]" < (b) (6) "Lane, Cliff (NIH/NIAID) [E]" < (b) (6) "Patterson, Amy (NIH/NHLBI) [E]" < (b) (6) "Parker, Ashley (NIH/OD) [E]" < (b) (6)
Subject: RE: Input requested on STORM

Larry,
We are definitely interested in talking with them. Could you provide the connection?

Thanks,
Joni

From: Tabak, Lawrence (NIH/OD) [E] < (b) (6)
Sent: Sunday, January 31, 2021 7:32 AM
To: Rutter, Joni (NIH/NCATS) [E] < (b) (6) Collins, Francis (NIH/OD) [E] < (b) (6) Freire, Maria (FNIH) [T] < (b) (6) Wholley, David (FNIH) [T] < (b) (6) Anderson, James (NIH/OD) [E] < (b) (6) Lane, Cliff (NIH/NIAID) [E] < (b) (6) Patterson, Amy (NIH/NHLBI) [E] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6)
Subject: Re: Input requested on STORM

Joni,
Is STORM something NCATS would be interested in talking to the investigator about?
Thanks
larry

From: "Rutter, Joni (NIH/NCATS) [E]" (b) (6)
Date: Friday, January 29, 2021 at 12:05 PM
To: "Tabak, Lawrence (NIH/OD) [E]" (b) (6) Francis Collins (b) (6) "Freire, Maria (FNIH) [T]" (b) (6) , "Wholley, David (FNIH) [T]" (b) (6) "Anderson, James (NIH/OD) [E]" (b) (6) , "Lane, Cliff (NIH/NIAID) [E]" < (b) (6) >, "Patterson, Amy (NIH/NHLBI) [E]" <amy. (b) (6) "Parker, Ashley (NIH/OD) [E]" (b) (6)
Subject: RE: Input requested on STORM

Larry,
Agree with David regarding CURE ID. There are a few other resources that are complementary, listed below. STORM looks complementary, simple, and useful.

CURE ID

- https://cure.ncats.io/
- It is an internet-based data repository developed as a collaboration between the U.S. Food and Drug Administration (FDA) and the National Center for Advancing Translational Sciences, a part of the National Institutes of Health (NCATS/NIH).
- It was developed with support from the Infectious Diseases Society of America (IDSA), the Centers for Disease Control and Prevention (CDC), and the World Health Organization (WHO). It gives the global clinical community the opportunity to report novel uses of existing drugs for patients with difficult-to-treat infectious diseases through a website, a smartphone or other mobile device.

TransNIH2 – (Not Public, see bullet in red)

- COVID-19 Clinical Trial Tracker (k/a "FDA Data Lake")
- The COVID-19 clinical trials data lake (originating at the FDA/OWS team) is a database with curated information from several large publicly available clinical trial registries including public data from ClinicalTrials.gov as well as the World Health Organization (WHO) International Clinical Trials Registry Program (ICTRP) and supplemental data from various other registries such as Australia/New Zealand, China, Germany, Iran, Netherlands, and EU.
- ***Current access group:*** NIH OD (Collins, Tabak, Parker, Culp, Gadbois), FNIH/ACT V leadership, ACTIV "War Room" attendees, TransNIH2 working group. Accepting new user requests on approximately February 11, 2021.

OpenData Portal

- https://opendata.ncats.nih.gov/covid19/
- A collection of datasets screening a panel of SARS-CoV-2-related assays against all approved drugs
- These datasets, as well as the assay protocols used to generate them, are being made immediately available to the scientific community on this site as these screens are completed

National COVID Cohort Collaborative (N3C)

- https://ncats.nih.gov/n3c
- A near real-time research resource of real world EHR data that can, among other uses, be used for looking at prescribing practices for treating COVID-19.

NCATS Inxight: Drugs (*not COVID specific*)

- https://drugs.ncats.io/
- Online portal that aggregates reliable, curated drug development data from multiple existing sources, all in one place.

Joni

From: Tabak, Lawrence (NIH/OD) [E] (b) (6)
Sent: Friday, January 29, 2021 8:38 AM
To: Collins, Francis (NIH/OD) [E] < (b) (6) gov>, Freire, Maria (FNIH) [T] < (b) (6) Wholley, David (FNIH) [T] < (b) (6) Anderson, James (NIH/OD) [E] < (b) (6) Lane, Cliff (NIH/NIAID) [E] (b) (6) Patterson, Amy (NIH/NHLBI) [E] (b) (6) ; Parker, Ashley (NIH/OD) [E] (. Rutter, Joni (NIH/NCATS) [E] (b) (6)
Subject: Input requested on STORM
Importance: High

The Office of the Secretary, has asked if the STORM database (developed at UPENN) - https://public.tableau.com/profile/matt.chadsey#!/vizhome/STORMDB/STORMDashboard, which is designed to track all reported off label and experimental drug use in COVID19 to help physicians treating COVID 19 patients know what treatments are most likely to help their patients, and to help researchers appropriately prioritize clinical trial, would be useful? Or are there other systems already serving a similar function?

Thanks,
Larry

From: Collins, Francis (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=410E1CA313F44CED9938E50D2FF0B6C2-COLLINSF]
Sent: 1/20/2021 7:30:44 PM
To: Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Menetski, Joseph (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5001af52dc4a427ea3d34f1e072f8cb7-menetskijp]; Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Austin, Christopher (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=17597cabc42247548e596778304f781f-austinc]; Lane, Cliff (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]; Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]; Patterson, Amy (NIH/NHLBI) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=afad1ca74b3e449d8b4f3191d65bb70f-pattersa]
CC: Shapiro, Neil (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a13c20d004cb413b9484d6343b5f3fa6-shapironk]
Subject: FW: Approved Funding Memo - Therapeutics - Variant Tracking & MAb-Vx Studies
Attachments: 20210119_Funding Memo_Therapeutics Variant Tracking and mAb-Vx Studies.pdf; Re. URGENT: FM Status Update

Happy to see this The second attachment says that Paul Mango approved the funds for the mutation tracking and functional analysis project.

FC

From: Bugin, Kevin < (b) (6)
Sent: Wednesday, January 20, 2021 11:04 AM
To: Collins, Francis (NIH/OD) [E] < (b) (6) Shapiro, Neil (NIH/OD) [E] < (b) (6)
Cc: Woodcock, Janet (FDA/CDER) < (b) (6)
Subject: FW: Approved Funding Memo - Therapeutics - Variant Tracking & MAb-Vx Studies

For your records!!

Neil,
Please see my email from Saturday morning. We should get to work on the accounting of how this will be dispersed. There are some new rules from OMB that ASFR has to follow. Lester will guide us but we have to work with him. Thanks,

Kevin

From: Windom, Robert (OS/ASPR/IO) < (b) (6)
Sent: Wednesday, January 20, 2021 10:58 AM
Cc: Kadlec, Robert P (OS) (b) (6) >; Disbrow, Gary (OS) (b) (6) ; Petillo, Jay (OS) (b) (6) ; Bugin, Kevin < (b) (6) Hayes, Jonathan H (OS) (b) (6) >; Hassell, David (OS) (b) (6) >; Woodcock, Janet < (b) (6) Cash, Lester (OS) < (b) (6) >; Overstreet, Elizabeth (OS) < (b) (6)
Subject: Approved Funding Memo Therapeutics Variant Tracking & MAb Vx Studies

Good morning,

The attached FM is approved, with email confirmation - $49.4M for Variant Tracking & mAb Vx/ nteraction studies.

v/r
raw

CAPT Robert A. Windom
ASPR Liaison – Federal COVID-19 Response
HHH – Suite 638G
200 Independence Avenue SW
Washington, DC 20201
(b) (6)
Desk: (b) (6)
Mobile: (b) (6)

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— Denze W.

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From: Windom, Robert (OS/ASPR/IO)
Sent: Friday, January 15, 2021 4:35 PM
To: Sherman, Susan (HHS/OGC) (b) (6) >; Cochran, Norris (HHS/ASFR) (b) (6)
Cash, Lester (HHS/ASFR) (b) (6)
Cc: Kadlec, Robert (OS/ASPR/IO) (b) (6) Disbrow, Gary (OS/ASPR/BARDA) (b) (6)
Petillo, Jay (OS/ASPR/MFHC) (b) (6) Bugin, Kevin (FDA/CDER) < (b) (6) >; Hayes,
Jonathan (OS/ASPR/IO) (b) (6) ; Hassell, David (Chris) (OS/ASPR/IO) (b) (6) >;
Woodcock, Janet (FDA/CDER) < (b) (6)
Subject: ACTION: Funding Memo - Therapeutics - Variant Tracking & MAb-Vx Studies

Good afternoon,

Attached please find a funding memo on behalf of the Therapeutics team to request $49.4M for Variant Tracking & mAbx/Interaction studies.

Per our process I am sending to ASFR and HHS Counsel for concurrent review. Once I hear back, I will route for signature.

v/r
raw

CAPT Robert A. Windom
Operation Warp Speed
ASPR Fusion Cell
HHH – Suite 638G
200 Independence Avenue SW
Washington, DC 20201
(b) (6)
Desk: (b) (6)
Mobile: (b) (6)

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— Denze W.

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From: Wholley, David (FNIH) [T] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=CD9E702FCF28414883D0B6996D677257-WHOLLEYD]
Sent: 12/21/2020 3:29:21 AM
To: Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]; Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Lane, Cliff (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]; Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]; Austin, Christopher (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=17597cabc42247548e596778304f781f-austinc]; Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]; Lane, Cliff (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]
CC: Menetski, Joseph (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5001af52dc4a427ea3d34f1e072f8cb7-menetskijp]
Subject: FW: N501Y variant in the UK

Here is the answer from the perspective of our preclinical WG so far.

From: Menetski, Joseph (FNIH) [T] < (b) (6)
Sent: Sunday, December 20, 2020 4:34 PM
To: Wholley, David (FNIH) [T] < (b) (6) Freire, Maria (FNIH) [T] < (b) (6)
Cc: Menetski, Joseph (FNIH) [T] < (b) (6)
Subject: FW: N501Y variant in the UK

I believe a short discussion around this mutation was in my highlight to War room on Friday, but there wasn't much detail because there isn't much definitive. The biggest worry is that it appear to come from no where and is spread ng fast. So most of the current questions in the group are about transmissibility and virulence.

The short answer for therapeutic efficacy is, influence on vaccines and therapeutics needs to be tested.

However:
We heard from Mikael that the vaccines are not showing any resistance mutations showing up in their testing (we don't know if this exact mutation has been tested). CDC does not have a clone of the isolate as of this morning.
For therapeutics, the actual residue (501) is not described as part of any binding epitopes or in the selected mutations (where available) for any of the agents that are currently in development by ACTIV. Again, we can't really know without wet lab testing (binding studies and at least cell neutralization studies).

I can ask the team that has been meeting all weekend for their comments, if it is OK to share this request with them. They include folks from CDC, FDA, NIAID, NCATS, NCBI, Roche and Gilead.

Joe

From: Collins, Francis (NIH/OD) [E] (b) (6)
Sent: Sunday, December 20, 2020 4:06 PM
To: Wholley, David (FNIH) [T] (b) (6) Menetski, Joseph (FNIH) [T] <] (b) (6) Graham, Barney (NIH/VRC) [E] < (b) (6) ; Mascola, John (NIH/VRC) [E] (b) (6)

Cc: Fauci, Anthony (NIH/NIAID) [E] < (b) (6) Freire, Maria (FNIH) [T] (b) (6) , Lawrence (NIH/OD) [E] (b) (6) >; Austin, Christopher (NIH/NCATS) [E] (b) (6) ; Anderson, James (NIH/OD) [E] (b) (6) >; Patterson, Amy (NIH/NHLBI) [E] < (b) (6) Lane, Cliff (NIH/NIAID) [E] (b) (6) Parker, Ashley (NIH/OD) [E] (b) (6)
Subject: N501Y variant in the UK

Hi David, Joe, Barney, and John,

The N501Y variant in the spike protein has risen rapidly in frequency in the UK and is causing much alarm there about increased transmissibility, now causing 62% of cases in London. See https //www.wsj.com/articles/what we know about-the-new-covid-19-strain-in-england-11608423416 Has the ACTIV mutation tracking team already jumped on this to see what its effects on vaccines and mAbs might be? Have the VRC experts already done an assessment of this one?

Francis

From: Collins, Francis (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=410E1CA313F44CED9938E50D2FF0B6C2-COLLINSF]
Sent: 5/25/2020 1:14:46 PM
To: Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Lane, Cliff (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]; Austin, Christopher (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=17597cabc42247548e596778304f781f-austinc]; Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]
Subject: FW: OWS therapeutics updated NIH needs
Attachments: Integrated Operation Warp Speed Globa Budget Template - Therapeutics May24.x sx

FYI

From: Marston, Hilary (NIH/NIAID) [E] < (b) (6)
Sent: Sunday, May 24, 2020 7:00 PM
To: Bugin, Kevin (FDA/CDER) < (b) (6)
Cc: Woodcock, Janet (FDA/CDER) < (b) (6) Collins, Francis (NIH/OD) [E] < (b) (6) Fauci, Anthony (NIH/NIAID) [E] < (b) (6) Tabak, Lawrence (NIH/OD) [E] < (b) (6) Read, Sarah (NIH/NIAID) [E] < (b) (6)
Subject: OWS therapeutics updated NIH needs

Kevin –

Thanks again for coordinating this budget process. Drs. Collins, Tabak, Fauci, Gibbons, Austin met today and discussed the numbers and the attached reflects their consensus Apologies for the changes but these are important updates and all reflect urgent needs:

- First, the preclinical now includes the needs of the ACTIV therapeutics preclinical working group, encompassing multiple therapeutic categories. The total is now $250 for the low end (the high end estimates were from BARDA, I believe). We included some details in the notes column, but please let us know if you need more.
- We have moved ACTIV immunomodulator and ACTIV anticoagulation to Phase 3. The latter is broken into inpt ($40M) and outpt ($35M).
- The Program Management (now labelled "Clinical Trial Management") has been decreased significantly, because in speaking to the networks, most of those costs are baked into the trial costs.
- We have added ACTIV program management funds as a stand-alone line item to fill a critical budget need.

Thanks very much and please let me know if you have any questions.

Hilary

Hilary D. Marston, MD MPH

Medical Officer and Policy Advisor for Pandemic Preparedness
Immediate Office of the Director
National Institute of Allergy and Infectious Diseases
Cell: (b) (6)
Email: (b) (6)

Sent: 6/1/2020 4:49:09 AM
To: Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]
Subject: RE: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers
Attachments: Draft ACTIV slides Hever COVID Meeting June 2, 2020 060120.pptx

Hi Francis,

If you approve – attached is the updated version we can submit to Hever tomorrow?

Thanks,
Ashley

From: Parker, Ashley (NIH/OD) [E]
Sent: Sunday, May 31, 2020 10:53 PM
To: Collins, Francis (NIH/OD) [E] < (b) (6)
Subject: RE: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

Hi Francis,

Based on the mAb discussions/progress over the weekend, I've shared the attached updated version with Stacey and David for review. Sorry our emails must have been crossed. We can certainly delete the extras with the exception of the minimum entry criteria.

Thank you,
Ashley

From: Collins, Francis (NIH/OD) [E] < (b) (6)
Sent: Sunday, May 31, 2020 10:43 PM
To: Parker, Ashley (NIH/OD) [E] < (b) (6)
Subject: RE: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

Thanks, Ashley.

I made a slight change to slide 10, and got rid of all of the extras except slide 12. Fine to submit in the AM.

FC

From: Parker, Ashley (NIH/OD) [E] < (b) (6)
Sent: Friday, May 29, 2020 4:35 PM
To: Collins, Francis (NIH/OD) [E] < (b) (6)
Subject: FW: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

Pulling this to the top of your inbox.

Thanks,
Ashley

From: Parker, Ashley (NIH/OD) [E]
Sent: Friday, May 29, 2020 12:31 AM

To: Collins, Francis (NIH/OD) [E] < (b) (6)
Cc: Wholley, David (FNIH) [T] < (b) (6) Adam, Stacey (FNIH) [T] < (b) (6)
Subject: RE: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

Hi Francis,

Please see the attached slides for your Hever update, 6/2 with a focus on mAbs master protocols. I've shared the pre-read *JAMA* article on ACTIV with Morten and they've asked for final slides by COB today but no later than noon Monday.

With many thanks – David and Stacey have reviewed and provided edits.

We may have 2 slides too many but figured you may want to quickly show the current partners and structure for ACTIV. We standby for any additional changes.

Thanks,
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From: Parker, Ashley (NIH/OD) [E]
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To: Collins, Francis (NIH/OD) [E] < (b) (6) Wholley, David (FNIH) [T] < (b) (6)
Subject: RE: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

Yes, will do.

Thanks,
Ashley

From: Collins, Francis (NIH/OD) [E] < (b) (6)
Sent: Wednesday, May 27, 2020 10:39 AM
To: Parker, Ashley (NIH/OD) [E] < (b) (6) Wholley, David (FNIH) [T] < (b) (6)
Subject: RE: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

Thanks. Can you go ahead and send the JAMA article to Morten, I haven't done so.

From: Parker, Ashley (NIH/OD) [E] < (b) (6)
Sent: Wednesday, May 27, 2020 8:12 AM
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Subject: RE: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

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Attached is the JAMA article pre-read — due by COB tomorrow if you haven't shared with Morten.

Thanks,
Ashley

From: Collins, Francis (NIH/OD) [E] < (b) (6)
Sent: Monday, May 25, 2020 2:01 PM

To: Wholley, David (FNIH) [T] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6)
Subject: FW: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

See instructions below from Sogaard about the coming Hever meeting. All this seems a bit over the top in prescribing the format, but ok.

With just 15 minutes for the ACTIV presentation, I would think we should use 5 or 6 slides about the overall status of the effort, and then a final slide or two on the mAb trials (since that is the request for focus). It would be great to have help from you two for that.

For the pre-read, I would think the JAMA article would be just fine. If you agree, I can send that to Morten now.

FC

From: (b) (6) (b) (6)
Sent: Monday, May 25, 2020 12:58 PM
To: (b) (6) Collins, Francis (NIH/OD) [E] < (b) (6) Woodcock, Janet (FDA/CDER) < (b) (6) Stoffels, Paul [JJCUS] < (b) (6) Plump, Andrew < (b) (6)
Cc: (b) (6) (b) (6) jill < (b) (6) FMedSci Trevor (b) (6) (b) (6)
Subject: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

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As you know we are working to set up a 30 min check-in meeting end of next week for presenters. Awaiting scheduling of this and realizing that it may be challenging to get on all calendars – we wanted to provide some guide lines (but ultimately your call)

- The meeting is scheduled to be 105 min but we are hoping that we might end at 90 minutes if we are disciplined.
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Kindly submit slides to Morten Sogaard and Jill Payne cc to Mikael Dolsten and Trevor Jones

Best regards,
Morten on beha f of the team

Agenda for Hever Group video WebEx on 2nd June ~ 90 min discussion (planned for 105 min, but hoping to end early)

- Setting the stage (Mikael) *5 min*
- Update on coordination of US COVID Initiatives (Moncef Slaoui) *10 min*
- Update on Covid R&D consortium ...pre-circulated **Clinical Trial Acceleration Overview** Update (Andy Plump)....Update on ACTIV trials with focus on new mAb master protocol (Francis Collins tbc) *30 min (15- + 15)*
- **Regulatory streamlining** of COVID-19 Clinical Trials (Janet Woodcock w/ commentaries from key regulatory colleagues) *20 min*
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Sent: 6/1/2020 2:48:15 AM
To: Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]
Subject: RE: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers
Attachments: RE: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

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From: Collins, Francis (NIH/OD) [E] < (b) (6)
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Sent: Monday, May 25, 2020 2:01 PM
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From: Parker, Ashley (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=306B2244466140FAA95AAAAFE06EBD70-PARKERAS]
Sent: 6/1/2020 2:38:49 AM
To: Adam, Stacey (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dcd875f0679648859e1cf101c0943414-adamsj4]; Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]
CC: Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]
Subject: RE: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers
Attachments: Draft ACTIV slides Hever COVID Meeting June 2 2020ap-sjadw ap053120.pptx

Flag: Follow up

Hi Stacey and David,

I've updated Hever slides 9 and 10 for the mAb master protocols both outpatient and inpatient based on any updates I've seen over the weekend. I wasn't cc'd on the correspondence with the INSIGHT network and would like to ensure I didn't miss anything that happened today that should be included for Francis' meeting with the Hever group on Tues.

They've requested we submit final slides by noon tomorrow and Francis cc'd has not yet weighed in– would you be able to review slides 9 and 10? Particularly slide 10, has the INSIGHT MP group decided on endpoints for ACTIV-3?

Thanks!
Ashley

From: Adam, Stacey (FNIH) [T] < (b) (6)
Sent: Friday, May 29, 2020 12:20 AM
To: Parker, Ashley (NIH/OD) [E] < (b) (6)
Cc: Wholley, David (FNIH) [T] < (b) (6)
Subject: Re: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

Hi Ashley,

Sounds good I will see what ACTIV-3 has tomorrow.

Stacey

Sent from my iPhone. Please excuse the brevity and typos.

> On May 29, 2020, at 12:16 AM, Parker, Ashley (NIH/OD) [E] < (b) (6) wrote:
>
> Hi Stacey,
>
> We can hold off on placing the randomization figure in the slide to avoid any confusion and update if we have a visual before noon on Monday.
>
> Thank you again and have a good night!
> Ashley

From: Adam, Stacey (FNIH) [T] < (b) (6)
Sent: Friday, May 29, 2020 12:10 AM
To: Parker, Ashley (NIH/OD) [E] < (b) (6) Wholley, David (FNIH) [T] < (b) (6)
Subject: RE: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

Hi Ashley,

Yes, comment can be deleted.
As for the randomization schema, that actually belongs to the outpatient protocol ACTIV-2, but if you don't think anyone will notice that the scheme for ACTIV-3 might be slightly different, I think it is fine.

Thanks,
Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: (b) (6) | Mobile: (b) (6)

From: Parker, Ashley (NIH/OD) [E] < (b) (6)
Sent: Friday, May 29, 2020 12:05 AM
To: Adam, Stacey (FNIH) [T] (b) (6) Wholley, David (FNIH) [T] (b) (6)
Subject: RE: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

I've made some additional minor edits OK to include randomization scheme for slide 10? Please see attached.

Also, I plan to delete the comment in the 2nd bullet on this slide – assume this is worked out.

Thanks,
Ashley

From: Parker, Ashley (NIH/OD) [E]
Sent: Thursday, May 28, 2020 11:10 PM
To: Wholley, David (FNIH) [T] < (b) (6) rg>; Adam, Stacey (FNIH) [T] < (b) (6)
Subject: RE: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

Got it – thank you both.

Ashley

From: Wholley, David (FNIH) [T] < (b) (6)
Sent: Thursday, May 28, 2020 9:11 PM
To: Adam, Stacey (FNIH) [T] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6)
Subject: RE: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

Same as the one I just sent.

From: Adam, Stacey (FNIH) [T] < (b) (6)
Sent: Thursday, May 28, 2020 9:03 PM
To: Parker, Ashley (NIH/OD) [E] < (b) (6) Wholley, David (FNIH) [T] < (b) (6)
Subject: RE: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

Hi Ashley,

Sorry for the multiple emails, the large file is delaying the exchange.

Please use this version edited by both David and I for FC.

Thanks,
Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: (b) (6) | Mobile: (b) (6)

From: Parker, Ashley (NIH/OD) [E] < (b) (6)
Sent: Thursday, May 28, 2020 8:55 PM
To: Wholley, David (FNIH) [T] < (b) (6) Adam, Stacey (FNIH) [T] < (b) (6)
Subject: Re: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

Hi David and Stacey,

Checking to see if you or Stacey had edits to the slides before I send to Francis for review tonight. I'm thinking we should delete the placeholder slide for the mAb inpatient protocol — unless we'll have information before Monday morning.

Also, there was back and forth on the stats — current slide set has Bayesian model will be used but I thought I may have heard a different approach today.

Thoughts?

Thanks,
Ashley

Begin forwarded message:

> **From:** "Parker, Ashley (NIH/OD) [E]" < (b) (6)
> **To:** "Wholley, David (FNIH) [T]" < (b) (6)
> **Subject: Re: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers**
>
> Just making sure you saw this. Hever has asked for final materials by tomorrow preferably – need to send to FC for review after your team.
>
> Thanks!

Ashley

From: Parker, Ashley (NIH/OD) [E]
Sent: Thursday, May 28, 2020 1:20 AM
To: Wholley, David (FNIH) [T] < (b) (6) Adam, Stacey (FNIH) [T] < (b) (6)
Subject: RE: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

Hi David and Stacey,

Attached is a draft set of slides for the 15-min ACTIV update with the Hever group. I've rearranged the order a bit and placed the Tx clinical updates at the end of the presentation to avoid jumping around and transition directly to the mAb trials requested by the group. Happy to reorder if preferred but need to pass by your team before sending to FC for review later today – Hever has asked for slides preferably by COB Friday, no later than noon Monday.

On the mAb slides – I do not have any information on the inpatient mAb trial design etc., a placeholder slide is inserted if needed. Dolsten also asked about options for combination therapies – defer to your team if this should be depicted/included on the slides

Thanks,
Ashley

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Sent: Monday, May 25, 2020 2:01 PM
To: Wholley, David (FNIH) [T] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6)
Subject: FW. June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

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< (b) (6)
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Sent: 6/1/2020 12:52:32 PM
To: Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]; Adam, Stacey (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dcd875f0679648859e1cf101c0943414-adamsj4]; Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]
Subject: RE: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers
Attachments: ACTIV slides_Hever COVID Meeting June 2, 2020.pptx

Good morning,

Thank you Stacey. Attached is the version we plan to submit to Hever with the minor edits outlined below. Francis – look OK to send?

Thanks,
Ashley

From: Collins, Francis (NIH/OD) [E] < (b) (6)
Sent: Monday, June 1, 2020 7:57 AM
To: Adam, Stacey (FNIH) [T] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6) Wholley, David (FNIH) [T] < (b) (6)
Subject: RE: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

Thanks. Yean, I think that two step randomization might be a bit too weedy for the time I have available.

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Sent: Monday, June 1, 2020 7:52 AM
To: Collins, Francis (NIH/OD) [E] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6) Wholley, David (FNIH) [T] < (b) (6)
Subject: RE: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

Hi Francis,

The "n" stands for neutralizing. The ACTIV-3 team seem to prefer this designation versus just mAb to avoid confusion with non-SARS-CoV-2 targeting mAbs.

The two step randomization means you first get randomized to a particular drug, and then you get randomized between that drug and placebo. This is because the team has not yet been able to determine if all nMAb will be able to share the same placebo. If they can, you are correct this will be amended to a one-stage randomization. They are merely covering contingencies at the moment while we wait for the mAb Summit.

If discussing the two stage randomization is to weedy for this group, it would be perfectly fine to just say randomized between treatment arms and control.

I hope this helps,
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Director, Cancer
Research Partnerships

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Sent: Monday, June 1, 2020 5:15 AM
To: Adam, Stacey (FNIH) [T] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6) Wholley, David (FNIH) [T] < (b) (6)
Subject: RE: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

Thanks, Stacey.

For slide, please explain the use of the term nMAb. What's the "n" for? And I don't think I understand the two-step random zation. If you have two mAbs that are ready to go into the trial, just use a common control arm. What's the reason for the two steps?

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Best regards,
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Subject: RE: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers
Attachments: Draft ACTIV slides _Hever COVID Meeting June 2 2020ap-sjadw_ap053120.pptx

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Attachments: ACTIV slides_Hever COVID Meeting June 2, 2020.pptx

Good morning,

Attached is the version we plan to share with Hever including minor changes outlined below. Francis – look OK?

Thanks,
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Thanks. Yeah, I think that two step randomization might be a bit too weedy for the time I have available.

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Hi Francis,

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Subject: RE: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers
Attachments: Draft ACTIV slides _Hever COVID Meeting June 2 2020ap-sjadw_ap053120.pptx

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Subject: RE: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers
Attachments: Draft ACTIV slides Hever COVID Meeting June 2, 2020 060120.pptx

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To: Wholley, David (FNIH) [T] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6)
Subject: FW: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

See instructions below from (b) (6) about the coming Hever meeting. All this seems a bit over the top in prescribing the format, but ok.

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From: (b) (6) (b) (6)
Sent: Monday, May 25, 2020 12:58 PM
To: (b) (6) Collins, Francis (NIH/OD) [E] < (b) (6) Woodcock, Janet (FDA/CDER) < (b) (6) Stoffels, Paul [JJCUS] < (b) (6) Plump, Andrew (b) (6)
Cc:((b) (6) jill < (b) (6) FMedSci Trevor < (b) (6) (b) (6)
Subject: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

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Kindly submit slides to Morten Sogaard and Jill Payne cc to Mikael Dolsten and Trevor Jones

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Sent: 5/29/2020 4:02:40 AM
To: Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Adam, Stacey (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dcd875f0679648859e1cf101c0943414-adamsj4]
Subject: RE: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers
Attachments: Draft ACTIV slides Hever COVID Meeting June 2 2020ap-sjadw .pptx

I've made some additional minor edits. OK to include randomization scheme for slide 10? Please see attached.

Thanks,
Ashley

From: Parker, Ashley (NIH/OD) [E]
Sent: Thursday, May 28, 2020 11:10 PM
To: Wholley, David (FNIH) [T] < (b) (6) Adam, Stacey (FNIH) [T] < (b) (6)
Subject: RE: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

Got it – thank you both.

Ashley

From: Wholley, David (FNIH) [T] < (b) (6)
Sent: Thursday, May 28, 2020 9:11 PM
To: Adam, Stacey (FNIH) [T] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6)
Subject: RE: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

Same as the one I just sent.

From: Adam, Stacey (FNIH) [T] < (b) (6)
Sent: Thursday, May 28, 2020 9:03 PM
To: Parker, Ashley (NIH/OD) [E] < (b) (6) Wholley, David (FNIH) [T] < (b) (6)
Subject: RE: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

Hi Ashley,

Sorry for the multiple emails, the large file is delaying the exchange.

Please use this version edited by both David and I for FC.

Thanks,
Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: (b) (6) Mobile: (b) (6)

From: Parker, Ashley (NIH/OD) [E] < (b) (6)
Sent: Thursday, May 28, 2020 8:55 PM

To: Wholley, David (FNIH) [T] < (b) (6) Adam, Stacey (FNIH) [T] < (b) (6)
Subject: Re: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

Hi David and Stacey,

Checking to see if you or Stacey had edits to the slides before I send to Francis for review tonight. I'm thinking we should delete the placeholder slide for the mAb inpatient protocol — unless we'll have information before Monday morning.

Also, there was back and forth on the stats — current slide set has Bayesian model will be used but I thought I may have heard a different approach today.

Thoughts?

Thanks,
Ashley

Begin forwarded message:

> **From:** "Parker, Ashley (NIH/OD) [E]" < (b) (6)
> **To:** "Wholley, David (FNIH) [T]" < (b) (6)
> **Subject: Re: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers**
>
> Just making sure you saw this. Hever has asked for final materials by tomorrow preferably – need to send to FC for review after your team.
>
> Thanks!
> Ashley
>
> **From:** Parker, Ashley (NIH/OD) [E]
> **Sent:** Thursday, May 28, 2020 1:20 AM
> **To:** Wholley, David (FNIH) [T] < (b) (6) Adam, Stacey (FNIH) [T] < (b) (6)
> **Subject:** RE: June 2 HEVER COVID-19 call Slide logistics and guidance for speakers
>
> Hi David and Stacey,
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>
> On the mAb slides – I do not have any information on the inpatient mAb trial design etc., a placeholder slide is inserted if needed. Dolsten also asked about options for combination therapies – defer to your team if this should be depicted/included on the slides.
>
> Thanks,
> Ashley
>
> **From:** Collins, Francis (NIH/OD) [E] < (b) (6)
> **Sent:** Monday, May 25, 2020 2:01 PM

To: Wholley, David (FNIH) [T] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6)
Subject: FW: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

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Cc: (b) (6) (b) (6) jill < (b) (6) FMedSci Trevor < (b) (6) (b) (6)
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Sent: 5/28/2020 5:19:52 AM
Subject: RE: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers
Attachments: Draft ACTIV slides_Hever COVID Meeting June 2, 2020.pptx

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Cc'ing Stacey on the mAb slides – I do not have any information on the inpatient mAb trial design etc., a placeholder slide is inserted.

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To: Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Adam, Stacey (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dcd875f0679648859e1cf101c0943414-adamsj4]
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Attachments: Draft ACTIV slides Hever COVID Meeting June 2, 2020.pptx

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On the mAb slides – I do not have any information on the inpatient mAb trial design etc., a placeholder slide is inserted. Dolsten also asked about options for combination therapies – should we add this to the slides?

Happy to trim as well – 10 slides may be too many for 15 mins.

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Sent: 5/28/2020 5:07:59 AM
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To: Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Adam, Stacey (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dcd875f0679648859e1cf101c0943414-adamsj4]
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Attachments: Draft ACTIV slides Hever COVID Meeting June 2, 2020.pptx

Hi David and Stacey,

Attached is a draft set of slides for the 15-min ACTIV update with the Hever group. I've rearranged the order a bit and placed the Tx clinical updates at the end to avoid jumping around and transition directly to the mAb trials requested by the group. Happy to reorder if preferred but need to pass by your team before sending to FC for review later today – Hever has asked for slides preferably by COB Friday, no later than noon Monday.

On the mAb slides – I do not have any information on the inpatient mAb trial design etc , a placeholder slide is inserted. Dolsten also asked about options for combination therapies – should we add this to the slides?

Thanks,
Ashley

From: Collins, Francis (NIH/OD) [E] < (b) (6)
Sent: Monday, May 25, 2020 2:01 PM
To: Wholley, David (FNIH) [T] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6)
Subject: FW: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

See instructions below from (b) (6) about the coming Hever meeting. All this seems a bit over the top in prescribing the format, but ok.

With just 15 minutes for the ACTIV presentation, I would think we should use 5 or 6 slides about the overall status of the effort, and then a final slide or two on the mAb trials (since that is the request for focus). It would be great to have help from you two for that.

For the pre-read, I would think the JAMA article would be just fine. If you agree, I can send that to Morten now.

FC

From: (b) (6)
Sent: Monday, May 25, 2020 12:58 PM
To: (b) (6) Collins, Francis (NIH/OD) [E] < (b) (6) Woodcock, Janet (FDA/CDER) < (b) (6) Stoffels, Paul [JJCUS] < (b) (6) Plump, Andrew < (b) (6)
Cc: (b) (6) (b) (6) jill < (b) (6) FMedSci Trevor < (b) (6) (b) (6) (b) (6)
Subject: June 2 HEVER COVID-19 call - Slide logistics and guidance for speakers

Dear All,

As we are getting closer to our June 2 HEVER COVID-19 meeting we are working to shore up the logistics for the meeting.

To that end we would like to ask you to

- Indicate if you plan to circulate pre reads if you are could you kindly submit them by Thursday May 28th End of Day EDT – so we can collate and send them out to the full team.
- Submit presentation slides by Monday June 1 by noon EDT at the latest – so we can collate into a master deck for efficient running of the meeting on June 2.

As you know we are working to set up a 30 min check-in meeting end of next week for presenters. Awaiting scheduling of this and realizing that it may be challenging to get on all calendars – we wanted to provide some guide lines (but ultimately your call)

- The meeting is scheduled to be 105 min but we are hoping that we might end at 90 minutes if we are disciplined.
- For the presentation we would recommend a few set up slides leading to one discussion slides outlining on the key proposals for the HEVER+ group to align on, and more detailed information in the pre-read.

Kindly submit slides to Morten Sogaard and Jill Payne cc to Mikael Dolsten and Trevor Jones

Best regards,
Morten on beha f of the team

Agenda for Hever Group video WebEx on 2nd June ~ 90 min discussion (planned for 105 min, but hoping to end early)

- Setting the stage (b) (6) *5 min*
- Update on coordination of US COVID Initiatives (Moncef Slaoui) *10 min*
- Update on Covid R&D consortium ...pre-circulated **Clinical Trial Acceleration Overview** Update (Andy Plump)....Update on ACTIV trials with focus on new mAb master protocol (Francis Collins tbc) *30 min (15- + 15)*
- **Regulatory streamlining** of COVID-19 Clinical Trials (Janet Woodcock w/ commentaries from key regulatory colleagues) *20 min*
- **Data sharing** ... review and suggestions for the way forward (Andy Plump) and **Accumulus overview** incl. alignment w/ data repository landscape (Paul Stoffels) *40 min* (20 + 20)

From: Parker, Ashley (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=306B2244466140FAA95AAAAFE06EBD70-PARKERAS]
Sent: 8/31/2020 4:09:20 PM
To: George, Jill (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f90bffb4b3a2464382adc29b127aed4e-georgejil]
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

No attachment.

From: George, Jill (NIH/OD) [E] < (b) (6)
Sent: Monday, August 31, 2020 12:03 PM
To: Parker, Ashley (NIH/OD) [E] < (b) (6)
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

I was mostly glad to see that Stacey said you corrected the slides well!
But I don't think it has the fixes I made to slide 3. Can you replace this slide 3 with the one I sent?

From: Parker, Ashley (NIH/OD) [E] (b) (6)
Sent: Monday, August 31, 2020 12:00 PM
To: George, Jill (NIH/OD) [E] < (b) (6)
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

No visual edits?

From: George, Jill (NIH/OD) [E] < (b) (6)
Sent: Monday, August 31, 2020 11:54 AM
To: Parker, Ashley (NIH/OD) [E] (b) (6)
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Nice!

From: Adam, Stacey (FNIH) [T] (b) (6)
Sent: Monday, August 31, 2020 11:53 AM
To: Parker, Ashley (NIH/OD) [E] (b) (6) Menetski, Joseph (FNIH) [T] < (b) (6)
Cc: George, Jill (NIH/OD) [E] (b) (6)
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Hi Ashley,

These now look correct to me if Joe does not have any further changes.

Thanks,
Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: (b) (6) , Mobile: (b) (6)

From: Parker, Ashley (NIH/OD) [E] (b) (6)
Sent: Monday, August 31, 2020 11:43 AM
To: Adam, Stacey (FNIH) [T] (b . Menetski, Joseph (FNIH) [T] (b) (6)
Cc: George, Jill (NIH/OD) [E] (b) (6)
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Hi Stacey,

I greatly appreciate the notes and you identifying the issue with the table. Attached is a clean vers on of both the PP and table. Once you've cleared we will clean up and send to FC for final review and get this to Hever.

Thanks,
Ashley

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Again, Joe and I can work through that this morning, but I am just curious how we propose to represent this, especially if you are going to list the specific targets themselves and not just perhaps color code them one versus the other.

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Director, Cancer
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Direct: (b) (6) | Mobile: (b) (6)

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Cc: Menetski, Joseph (FNIH) [T] < (b) (6)
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

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Thanks,
Ashley

From: Adam, Stacey (FNIH) [T] (b) (6)
Sent: Monday, August 31, 2020 8:36 AM
To: Parker, Ashley (NIH/OD) [E] < (b) (6)
Cc: Menetski, Joseph (FNIH) [T] (b) (6) >
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Hi Ashley,

I am now at my computer, sorry I was trekking to and from the gym this morning so was on my phone earlier. Do you need some assistance modifying the slides still or is there anything you still need from Joe and I?

Thanks,
Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: (b) (6) . Mobile: (b) (6)

From: Parker, Ashley (NIH/OD) [E] (b) (6)
Sent: Monday, August 31, 2020 7:48 AM
To: Adam, Stacey (FNIH) [(
Cc: Menetski, Joseph (FNIH) [T] (b) (6)
Subject: Re: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Sorry I forgot to mention there is no true back up slides — FC's slides will be merged with a larger presentation with other speakers.

Thanks,
Ashley

On Aug 31, 2020, at 7:44 AM, Parker, Ashley (NIH/OD) [E] (b) (6) > wrote:

> Thanks, Stacey! We will now have 17 no go's for wave 2 or there are 2 other compounds to replace these if the total is in fact 19 for wave 2?
>
> Thanks,
> Ashley
>
> On Aug 31, 2020, at 7:35 AM, Adam, Stacey (FNIH) [T] < (b) (6) wrote:
>
> > Hi Ashley,
> >
> > The duplicates should remain in the "Defer" category.
> >
> > I would just split the no-go to a separate slide. Abs move it to back up.
> >
> > Joe, would you agree?
> >
> > Thanks,
> > Stacey
> >
> > Sent from my iPhone. Please excuse the brevity and typos.

On Aug 31, 2020, at 7:13 AM, Parker, Ashley (NIH/OD) [E]
(b) (6) > wrote:

Yes, I agree and we can split slide 6 into two slides. I will standby for the other responses from Joe and Stacey before making the final edits.

Thanks,
Ashley

On Aug 31, 2020, at 5:13 AM, Collins, Francis (NIH/OD) [E]
(b) (6) > wrote:

> Thanks for pulling this together at 3 AM (!), Ashley. I'll wait to see what Joe and Stacey want to do about a final version. Slide 6 is going to be hard for people to read because of the large amount of information and the small font – might this need to be broken into two slides?
>
> FC
>
> **From:** Parker, Ashley (NIH/OD) [E]
> (b) (6)
> **Sent:** Monday, August 31, 2020 3 03 AM
> **To:** Collins, Francis (NIH/OD) [E] < (b) (6)
> Wholley, David (FNIH) [T] < (b) (6)
> Menetski, Joseph (FNIH) [T] (b) (6)
> Adam, Stacey (FNIH) [T] (b) (6)
> **Cc:** George, Jill (NIH/OD) [E] < (b) (6)
> **Subject:** RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides
>
> Hi Francis et al.,
>
> Attached is a revised version with the timelines of review for waves 1-3 prioritization efforts and the MOAs for most compounds. Joe – do we have information on viral and host targets? If so, please send and I can add this info to slides 5-7.
>
> I found two duplications (b) (4) and (b) (4) listed in both deferred and NO-GO) on slide 6 and need clarification on these as well.
>
> Otherwise does this set look closer to what you need for Hever? We will clean these up for visual purposes as well.
>
> Thanks,
> Ashley

From: Parker, Ashley (NIH/OD) [E]
Sent: Sunday, August 30, 2020 2:28 PM
To: Collins, Francis (NIH/OD) [E] (b) (6)
Wholley, David (FNIH) [T] < (b) (6)
Menetski, Joseph (FNIH) [T] (b) (6)
Adam, Stacey (FNIH) [T] (b) (6)
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Hi Francis,

We will take care of it and send a version back to you for review.

Thanks,
Ashley

From: Collins, Francis (NIH/OD) [E]
(b) (6)
Sent: Sunday, August 30, 2020 2:26 PM
To: Parker, Ashley (NIH/OD) [E]
(b) (6) ; Wholley, David (FNIH) [T]
< (b) (6) Menetski, Joseph (FNIH) [T]
(b) (6) >; Adam, Stacey (FNIH) [T]
< (b) (6)
Subject: FW: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Is it possible to group the antivirals from Waves 1 – 3 with these categories? Aren't they mostly "known viral targets"?

FC

From: Dolsten, Mikael (b) (6)
Sent: Sunday, August 30, 2020 10:56 AM
To: Collins, Francis (NIH/OD) [E] (b) (6)
Cc: Sogaard, Morten (b) (6) >;
Parker, Ashley (NIH/OD) [E] (b) (6)
George, Jill (NIH/OD) [E] (b) (6) ; Trevor Jones < (b) (6)
(b) (6) ; Geoff Frew
< (b) (6)
Subject: Re: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Good suggestion

Maybe we can group drugs to be tested in order to make cross presenter summary

Known viral targets

Host targets
Unknown MOA

Or any other matrix you prefer

Sent from my iPhone

> On Aug 30, 2020, at 09:49, Collins, Francis (NIH/OD) [E] (b) (6) > wrote:
>
> Hi (b) (6)
>
> I'd be glad to provide a brief summary of the extensive prioritization process that ACTIV is following for antivirals. I could present this with a few slides in about five minutes. But this would fit much better as part of the session with Plump, Bradner, and Hudson, rather than inserted in the Discussion at the end. Might that rearrangement be possible?
>
> Ashley can get slides to you by tomorrow.
>
> Francis
>
> **From:** (b) (6) < (b) (6)
> **Sent:** Sunday, August 30, 2020 9:16 AM
> **To:** Collins, Francis (NIH/OD) [E] (b) (6)
> **Cc:** Parker, Ashley (NIH/OD) [E] < (b) (6) George, Jill (NIH/OD) [E] (b) (6) ; (b) (6)
>
> < (b) (6) (b) (6) ; Geoff Frew < (b) (6) (b) (6) (b) (6)
> **Subject:** HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Dear Francis

I hope this e-mail is reaching you well.

I understand from Trevor that he had agreed with you to do a quick update on antivirals ACTIV activities and plans as part of the discussion session in Wednesday session.

So just checking in if you would plan to have pre-read slides, and also if you plan to have presentation slides or run the discussion without slides?
I think planning for ~ 5 minutes so as part of the discussion probably will be appropriate. We only have 1 hour for this next meeting – so a bit shorter than previous meetings.

It would be great if you could let us know if you plan to have presentations slides so that we can integrate those.

Also if Ashley could help send pre-read slides to myself and Jill cc to Trevor ideally by Monday 5 pm EST.

Please, see current draft agenda below.

Looking forward to an exciting discussion.

Best wishes on behalf of Mikael and Trevor,
Morten

<image001.jpg>

From: Parker, Ashley (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=306B2244466140FAA95AAAAFE06EBD70-PARKERAS]
Sent: 8/31/2020 2:41:13 PM
To: George, Jill (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f90bffb4b3a2464382adc29b127aed4e-georgejil]
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Yes working on it.

From: George, Jill (NIH/OD) [E] < (b) (6)
Sent: Monday, August 31, 2020 10:39 AM
To: Parker, Ashley (NIH/OD) [E] < (b) (6)
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Hi Ashley,
I've toyed with slide 3 a bit. The charts seem to be images that I can't easily edit. Let me know when/if I can be of any help once you get the data straightened out. Phew. I'm exhausted for you!
Jill

From: Adam, Stacey (FNIH) [T] (b) (6)
Sent: Monday, August 31, 2020 10:15 AM
To: Parker, Ashley (NIH/OD) [E] (b) (6) >; Menetski, Joseph (FNIH) [T] (b) (6)
Cc: George, Jill (NIH/OD) [E] (b) (6)
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Direct: (b) (6) | Mobile: (b) (6)

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Sent: Monday, August 31, 2020 9:55 AM
To: Menetski, Joseph (FNIH) [T] < (b) (6) Adam, Stacey (FNIH) [T] < (b) (6)
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Research Partnerships
Direct: (b) (6) | Mobile: (b) (6)

From: Parker, Ashley (NIH/OD) [E] < (b) (6)
Sent: Monday, August 31, 2020 7:48 AM
To: Adam, Stacey (FNIH) [T] (b) (6)
Cc: Menetski, Joseph (FNIH) [T] (b) (6)
Subject: Re: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Sorry I forgot to mention there is no true back up slides — FC's slides will be merged with a larger presentation with other speakers.

Thanks,
Ashley

On Aug 31, 2020, at 7:44 AM, Parker, Ashley (NIH/OD) [E] < (b) (6) wrote:

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Joe, would you agree?

Thanks,
Stacey

Sent from my iPhone. Please excuse the brevity and typos.

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>
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> Ashley
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> >
> > FC
> >
> > **From:** Parker, Ashley (NIH/OD) [E] < (b) (6)
> > **Sent:** Monday, August 31, 2020 3:03 AM
> > **To:** Collins, Francis (NIH/OD) [E] (b) (6) ; Wholley, David (FNIH) [T] (b) (6) ; Menetski, Joseph (FNIH) [T] < (b) (6) Adam, Stacey (FNIH) [T] (b) (6)
> > **Cc:** George, Jill (NIH/OD) [E] (b) (6)
> > **Subject:** RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides
> >
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Ashley

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Sent: Sunday, August 30, 2020 2:28 PM
To: Collins, Francis (NIH/OD) [E] (b) (6)
Wholley, David (FNIH) [T] (b) (6)
Menetski, Joseph (FNIH) [T] (b) (6) ;
Adam, Stacey (FNIH) [T] (b) (6)
Subject: RE. [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Hi Francis,

We will take care of it and send a version back to you for review.

Thanks,
Ashley

From: Collins, Francis (NIH/OD) [E]
(b) (6) >
Sent: Sunday, August 30, 2020 2:26 PM
To: Parker, Ashley (NIH/OD) [E]
(b) (6) ; Wholley, David (FNIH) [T]
< (b) (6) >; Menetski, Joseph (FNIH) [T]
(b) (6) Adam, Stacey (FNIH) [T]
(b) (6) >
Subject: FW: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Is it possible to group the antivirals from Waves 1 – 3 with these categories? Aren't they mostly "known viral targets"?

FC

From: (b) (6)
Sent: Sunday, August 30, 2020 10:56 AM
To: Collins, Francis (NIH/OD) [E] (b) (6)
Cc: (b) (6)
Parker, Ashley (NIH/OD) [E] < (b) (6)
George, Jill (NIH/OD) [E] (b) (6) >; Trevor Jones (b) (6)
(b) (6) ; Geoff Frew
(b) (6)
Subject: Re: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Good suggestion

Maybe we can group drugs to be tested in order to make cross presenter summary

Known viral targets
Host targets
Unknown MOA

Or any other matrix you prefer

Sent from my iPhone

> On Aug 30, 2020, at 09:49, Collins, Francis (NIH/OD) [E] < (b) (6) wrote:
>
> Hi (b) (6)
>
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>
> Ashley can get slides to you by tomorrow.
>
> Francis
>
> **From:** (b) (6) (b) (6)
> **Sent:** Sunday, August 30, 2020 9:16 AM
> **To:** Collins, Francis (NIH/OD) [E] < (b) (6)
> **Cc:** Parker, Ashley (NIH/OD) [E] < (b) (6) ; George, Jill (NIH/OD) [E] (b) (6) (b) (6) (b) (6) Trevor Jones (b) (6) >;

(b) (6) ; Geoff Frew
(b) (6) >;
(b) (6)
(b) (6)

Subject: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Dear Francis

I hope this e-mail is reaching you well.

I understand from Trevor that he had agreed with you to do a quick update on antivirals ACTIV activities and plans as part of the discussion session in Wednesday session.

So just checking in if you would plan to have pre-read slides, and also if you plan to have presentation slides or run the discussion without slides?
I think planning for ~ 5 minutes so as part of the discussion probably will be appropriate. We only have 1 hour for this next meeting – so a bit shorter than previous meetings.

It would be great if you could let us know if you plan to have presentations slides so that we can integrate those.

Also if Ashley could help send pre-read slides to myself and Jill cc to Trevor ideally by Monday 5 pm EST

Please, see current draft agenda below.

Looking forward to an exciting discussion.

Best wishes on behalf of Mikael and
(b) (6)

<image001.jpg>

From: Parker, Ashley (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=306B2244466140FAA95AAAAFE06EBD70-PARKERAS]
Sent: 8/31/2020 2:16:38 PM
To: Menetski, Joseph (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5001af52dc4a427ea3d34f1e072f8cb7-menetskijp]
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

I was counting on FNIH to confirm – see note from Stacey.

From: Menetski, Joseph (FNIH) [T] < (b) (6)
Sent: Monday, August 31, 2020 10:13 AM
To: Parker, Ashley (NIH/OD) [E] < (b) (6)
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Ashley,
Which 2 are missing? We have a few situations where the same compound was submitted by multiple separate sponsors, that may make the simple summing of numbers more tricky?

We can provide a better answer if we have the names of the outliers.

Joe

From: Parker, Ashley (NIH/OD) [E] < (b) (6)
Sent: Monday, August 31, 2020 9:55 AM
To: Menetski, Joseph (FNIH) [T] (b) (6) ; Adam, Stacey (FNIH) [T] < (b) (6)
Cc: George, Jill (NIH/OD) [E] (b) (6)
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Thanks, Joe and Stacey. Attached is the revised slide set and we can share the attached summary Dolsten has requested w/ the host vs. directed as a separate attachment.

There are 2 agents on the list (table) that are not accounted for based on the complete list Joe provided (56 total) – I assume 2 compounds that should go in the NO GO section for wave 2. Can you please let me know where the discrepancy is here and I will add those to where they belong?

Once we have this – we can clean the slides up for visual edits.

Thanks,
Ashley

From: Menetski, Joseph (FNIH) [T] (b) (6)
Sent: Monday, August 31, 2020 9:21 AM
To: Adam, Stacey (FNIH) [T] (b) (6) ; Parker, Ashley (NIH/OD) [E] < (b) (6)
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

I think in most cases I left the Target as part of the MOA. Looking at the slides, I think that the MOA that was used was the short one, that was more general. As Stacey says below, if it is direct acting and inhibits a protease, it is the viral protease, etc.

Based on the MOA, you can see that the target is either host or one of the main viral proteins.

It would be fairly easy to go through and highlight Host versus direct (most are host). Maybe separate viral protease and polymerase. Maybe using color coding.

It would be helpful to know how the information is intended to be used or interpretation that Francis wants to make.

Joe

From: Adam, Stacey (FNIH) [T] < (b) (6)
Sent: Monday, August 31, 2020 8:53 AM
To: Parker, Ashley (NIH/OD) [E] < (b) (6)
Cc: Menetski, Joseph (FNIH) [T] (b) (6)
Subject: RE: [EXTERNAL] RE: HEVER COVID 19 Antivirals meeting Sept 2 Slides

Hi Ashley,

Forgive me, but guess I am trying to understand what providing the specific target does on top of the fact that we have provided the MOA, and in Joe's spreadsheet that he sent last night he had coded the agents as either direct viral targeting or host targeting.

Joe, maybe this is my lack of knowledge in virology, but if we know it is a viral targeting agent and the MOA is that it inhibits a specific protease, is that not sufficient for the "target"? If so, then I think we have provided what Dolsten is asking for. If not then for some of the broad mechanistic actors, I am not sure we will have this information. Apologies, if I am missing some nuance.

Thanks,
Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: (b) (6) Mobile: (b) (6)

From: Parker, Ashley (NIH/OD) [E] < (b) (6)
Sent: Monday, August 31, 2020 8:47 AM
To: Adam, Stacey (FNIH) [T] (b) (6)
Cc: Menetski, Joseph (FNIH) [T] (b) (6)
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Hi Stacey,

Should we propose including a chart of the antivirals with the targets, MOU, as a separate attachment? If so, could you provided this and I can let FC know that's the plan. I have no preference here but want to ensure we provide what Dolsten has requested.

I will share the revised sl des once we are done editing.

Thanks,
Ashley

From: Adam, Stacey (FNIH) [T] <(
Sent: Monday, August 31, 2020 8:42 AM

To: Parker, Ashley (NIH/OD) [E] (b) (6)
Cc: Menetski, Joseph (FNIH) [T] < (b) (6)
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Hi Ashley,

Given all of the information already on these slides and the worry that they are busy, do we really want to try to fit the category of host-targeted versus viral targeted on these slides?
Again, Joe and I can work through that this morning, but I am just curious how we propose to represent this, especially if you are going to list the specific targets themselves and not just perhaps color code them one versus the other.

Thanks,
Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: (b) (6) Mobile: (b) (6)

From: Parker, Ashley (NIH/OD) [E] (b) (6) >
Sent: Monday, August 31, 2020 8:39 AM
To: Adam, Stacey (FNIH) [T] (b) (6)
Cc: Menetski, Joseph (FNIH) [T] (b) (6)
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Hi Stacey,

I am modifying the slides but I still do not have the viral and host targets for these compounds. Can I send the excel spreadsheet for these to be added or do we not have those?

Thanks,
Ashley

From: Adam, Stacey (FNIH) [T] (b) (6)
Sent: Monday, August 31, 2020 8:36 AM
To: Parker, Ashley (NIH/OD) [E] < (b) (6)
Cc: Menetski, Joseph (FNIH) [T] < (b) (6)
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Hi Ashley,

I am now at my computer, sorry I was trekking to and from the gym this morning so was on my phone earlier.
Do you need some assistance modifying the slides still or is there anything you still need from Joe and I?

Thanks,
Stacey

Stacey J. Adam, PhD
Director, Cancer
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Please, see current draft agenda below.

Looking forward to an exciting discussion.

Best wishes on behalf of (b) (6) and (b) (6)

<image001.jpg>

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Sent: 8/28/2020 8:09:54 PM
To: Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]
CC: Adam, Stacey (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dcd875f0679648859e1cf101c0943414-adamsj4]; Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]
Subject: RE: ACTIV LT Prioritization Slide

Thank you for doing this, it is a great start for us (sorry, I clicked too early)

joe

From: Parker, Ashley (NIH/OD) [E] < (b) (6)
Sent: Friday, August 28, 2020 3:46 PM
To: Menetski, Joseph (FNIH) [T] < (b) (6)
Cc: Adam, Stacey (FNIH) [T] < (b) (6) Wholley, David (FNIH) [T] < (b) (6)
Subject: RE: ACTIV LT Prioritization Slide

Hi Joe,

I found a very nice summary slide in the back pocket of the clinical Tx WG section for the antiviral prioritization (slide 8). It was missing 2 antivirals that were in the primary slide deck so I've added those.

Attached is a draft set that Francis could use for Hever w/ the plug to submit antivirals to the RedCap survey (slide 10). Could you and Stacey review and make any edits/additions (**slides 7-9 and any others that you want to edit**)?

I noticed there were 10 antivirals reviewed in the initial process (wave 1) with 3 chosen to defer for later prioritization (prior to implementat on of the RedCap survey). I assume these 3 agents were added to the pot w th others that came in through the RedCap portal for wave 2 (total of 36 antivirals) and it seems the group is currently undergoing review for wave 3. I've inserted a placeholder (slide 9) to be included but happy to remove if the group is not ready to share those.

Addit onal slides were placed in the back pocket for FC's background only.

Please let me know if this works – tomorrow is fine!

Thanks!
Ashley

From: Menetski, Joseph (FNIH) [T] (b) (6)
Sent: Friday, August 28, 2020 3:02 PM
To: Parker, Ashley (NIH/OD) [E] < (b) (6)
Cc: Adam, Stacey (FNIH) [T] (b ; Wholley, David (FNIH) [T] (b) (6)
Subject: RE: ACTIV LT Prioritization Slide

Dear Ashley,

I will put together a slide that includes all the evaluated antivirals, clinical and preclinical, and send that to you within the next 24 hours. Let me know if that is not going to work for you.

Thank you,

Joe

From: Parker, Ashley (NIH/OD) [E] (b) (6)
Sent: Friday, August 28, 2020 11:34 AM
To: Wholley, David (FNIH) [T] (b) (6) Menetski, Joseph (FNIH) [T] (b) (6)
Cc: Elsaid, Olivia (b) (6) >; Gonzalez, Nina (b) (6) >; Appell, Evan (b) (6) ; Adam, Stacey (FNIH) [T] (b) (6)
Subject: RE: ACTIV LT Prioritization Slide

Yes, thanks – had not made it to clinical antiviral slides yet!

Thanks!!
Ashley

From: Wholley, David (FNIH) [T] < (b) (6)
Sent: Friday, August 28, 2020 11:32 AM
To: Parker, Ashley (NIH/OD) [E] <as (b) (6) Menetski, Joseph (FNIH) [T] < (b) (6)
Cc: Elsaid, Olivia (b) (6) ; Gonzalez, Nina (b) (6) ; Appell, Evan (b) (6) Adam, Stacey (FNIH) [T] < (b) (6)
Subject: RE: ACTIV LT Prioritization Slide

Keeping Stacey in the loop. Antivirals are part of both the preclinical and clinical WG discussions.

From: Parker, Ashley (NIH/OD) [E] (b) (6)
Sent: Friday, August 28, 2020 11:32 AM
To: Menetski, Joseph (FNIH) [T] (b) (6) ; Wholley, David (FNIH) [T] (b) (6)
Cc: Elsaid, Olivia (b) (6) Gonzalez, Nina (b) (6) >; Appell, Evan (b) (6)
Subject: RE: ACTIV LT Prioritization Slide

Hi Joe,

Yes, Francis is presenting this to the Hever group for their antiviral meeting on Wed. They will likely want to see the antivirals that were deferred, assuming there are 3 antivirals deferred.

Can we please have a updated version unless you recommend he not share those antivirals that were deferred? I planned to remove the other compounds (immune modulators and other therapies) not pertinent to the discussion unless suggested otherwise.

Thanks,
Ashley

From: Menetski, Joseph (FNIH) [T] < (b) (6)
Sent: Friday, August 28, 2020 11:24 AM
To: Parker, Ashley (NIH/OD) [E] (b) (6) Wholley, David (FNIH) [T] (b) (6)
Cc: Elsaid, Olivia (b) (6) >; Gonzalez, Nina < (b) (6) . Appell, Evan (b) (6)
Subject: RE: ACTIV LT Prioritization Slide

Ashley,

The ones that were deferred from evaluation, mostly because they were too early, were not listed in the box. Only the ones in the box were evaluated in depth.

If that is not clear, please don't hesitate to contact me.

Joe

From: Parker, Ashley (NIH/OD) [E] (b) (6)
Sent: Friday, August 28, 2020 11:21 AM
To: Wholley, David (FNIH) [T] (b) (6)
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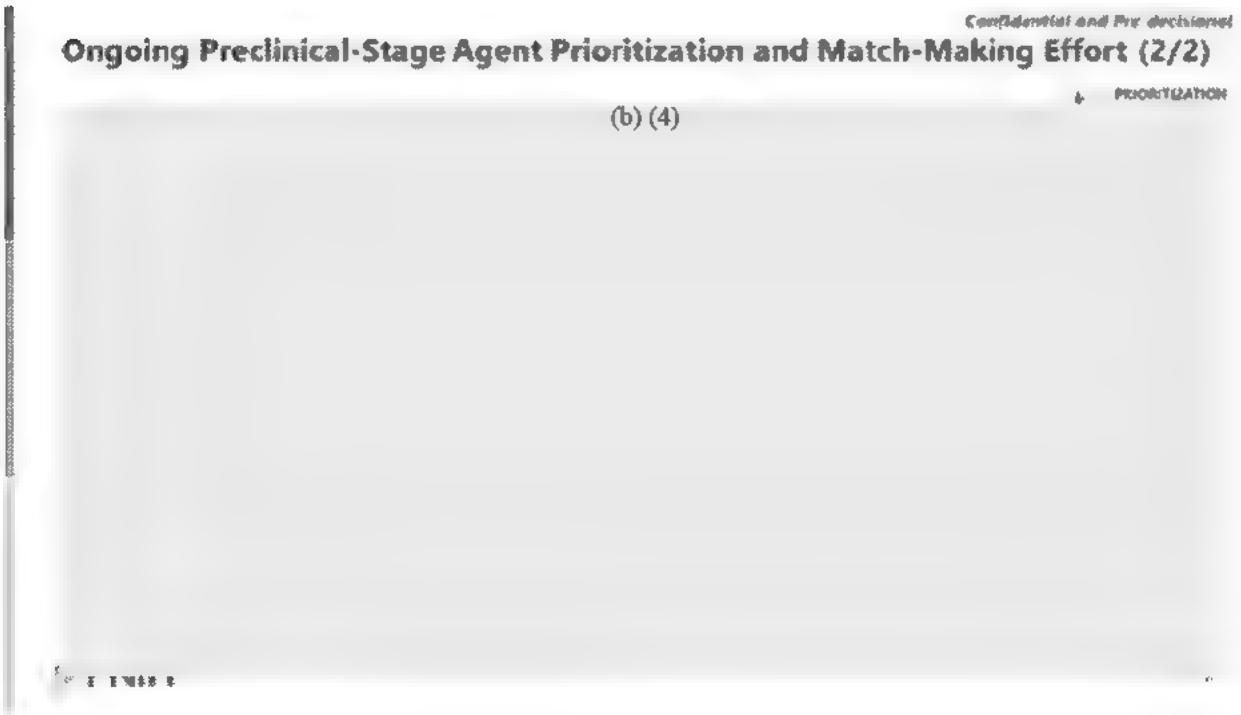
Subject: ACTIV LT Prioritization Slide

Hi David,

Per our discussion on the war room call this morning, I am pulling the antiviral data from the slides presented to the LT meeting on Wed. and noticed the number of antivirals in the wave 1 prioritization do not match the number of agents listed, please see below (7 antivirals with 4 antiviral agents listed)

This may have been corrected on the version displayed to the LT – could I please have a copy of the revised version?



Thanks,
Ashley

Ashley Parker, Ph.D.
Special Assistant to the NIH Director for Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)
Office of the Director | National Institutes of Health
Tel: (b) (6)


National Institutes of Health

From: Menetski, Joseph (FNIH) [T] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=5001AF52DC4A427EA3D34F1E072F8CB7-MENETSKIJP]
Sent: 8/31/2020 1:59:26 AM
To: Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]
CC: Adam, Stacey (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dcd875f0679648859e1cf101c0943414-adamsj4]; Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]
Subject: RE: Slides for Hever Antiviral Meeting
Attachments: DRAFT HEVER Sep. 2 2020 COVID-19 Antiviral Meeting_Presentation FRANCIS COLLINS v4.pptx; Table of Evaluated Antivirals for AP.xlsx

Ashley,

I have updated and modified the slides you sent to contain the MOAs for Wave 1. For Wave 2 and 3, I have added a note that the MOAs can be found in the back up slides.

I am also attaching an excel file with 2 tabs, one that has MOAs in very short form, the other has more detail. Can you put these into a form that is readable on a back up slide? That we the type of inhibitor and the MOA is provided, but doesn't take up all of Dr Collins' time for his update.

Best regards,
Joe

From: Parker, Ashley (NIH/OD) [E] < (b) (6)
Sent: Sunday, August 30, 2020 5:41 PM
To: Menetski, Joseph (FNIH) [T] < (b) (6)
Cc: Adam, Stacey (FNIH) [T] < (b) (6) Wholley, David (FNIH) [T] < (b) (6)
Subject: Re: Slides for Hever Antiviral Meeting

Hi Joe,

Sorry this is becoming more of a lift. I'm not sure if you have this for all antivirals but we did have MOAs in the back pocket of the first version of the PowerPoint file (pasted below) for approx 23 agents although some are blank and I think it's OK if the MOA is unknown. Could we use some modified version of these tables (minus scoring) and include the viral and host targets for waves 1-3?

We've learned we have to submit final slides for pre-reads by 5pm tomorrow. Tomorrow morning should be fine but it would need to be early enough for FC to clear before his day gets busy with meetings, like before 7:30am. Will this work? We'll handle any visual edits but please me know if I need to pull in extra hands to get this done.

Wave 2 Prioritization | Antivirals Round 1Results

Therapeutic Name	Mechanism of Action	Total Score	# of G
(b) (4)	Inhibits viral replication	16	
	Inhibits viral entry	14.8	

(b) (4)

HSP90 inhibitor	12	1
CK2 protein kinase inhibitor	9	1
DHODH inhibitor	8.2	1
Viricide	10	2
hnRNP A1 inhibitor	3.3	5
Inhibit viral entry	9.3	5
Inhibition of IMPalpha/beta1 mediated viral protein import	7.3	3
	5.2	2
cc-miR against COVID-19 gDNA	5	7

Therapeutic Name	Mechanism of Action	Total Scor
(b) (4)		8.3
	hnRNP A1 inhibitor	12.3
		11.7
	HSP90 inhibitor	8.7
		7.3
	DHODH inhibitor	7
	Inhibition of IMPalpha/beta1 mediated import of viral proteins	13.3
	Inhibits viral replication	5
	cc-miR against COVID-19 gDNA	2.7
	CK2 protein kinase inhibitor	2
	DHODH inhibitor	1.3
	Viricide	1.3

Thanks,
Ashley

Sent from iPhone

On Aug 30, 2020, at 4:34 PM, Menetski, Joseph (FNIH) [T] (b) (6) wrote:

Hi Ashley,

Collecting the MOAs will take some time because we have been collecting the data for review, not presentation, but we can work on trying to put something together.

We will try to get something to you tomorrow morning, if that is OK.

Joe

From: Parker, Ashley (NIH/OD) [E] (b) (6)
Sent: Sunday, August 30, 2020 2:44 PM
To: Menetski, Joseph (FNIH) [T] (b) (6)
Cc: Adam, Stacey (FNIH) [T] < (b) (6) Wholley, David (FNIH) [T] < (b) (6)
Subject: RE: S ides for Hever Antiviral Meeting

Hi Joe,

Thanks so much for the edits! Unfortunately, Dr. Collins will only have 5 mins to go through all the details – can we please add any preclinical compounds from slide 9 not already listed on slides 5-7 to the one of the decision charts on these slides? I understand the importance of knowing which antivirals are not clinic ready – can we add an asterisk by those compounds and place a footnote on the slide indicating "not clinic ready – preclinical"?

Also for the dates inserted can we specify what these dates represent? I've inserted the "reviewed" but please confirm or edit.

Per FC's note Dolsten has also asked for the viral targets, host targets, and MOA for the antivirals – can we please include this information on slides 5-7 or insert a table with this information, whatever is easier?

I am about to trave, and will be on the road for the next 5 hours but will be checking email again tonight once I have access to internet again.

Thanks,
Ashley

From: Menetski, Joseph (FNIH) [T] (b) (6)
Sent: Sunday, August 30, 2020 1:55 PM
To: Parker, Ashley (NIH/OD) [E] (b) (6)
Cc: Adam, Stacey (FNIH) [T] < (b) (6) Wholley, David (FNIH) [T] < (b) (6)
Subject: RE: S ides for Hever Antiviral Meeting

Ashley,

Stacey and I have made some edits. I have made the Slide 9 a bit more self-explanatory. However, it is up to you, this could still go into back up in case anyone asks about preclinical compounds.

Joe

From: Parker, Ashley (NIH/OD) [E] < (b) (6)
Sent: Sunday, August 30, 2020 1:12 AM

To: Collins, Francis (NIH/OD) [E] (b) (6)
Cc: Menetski, Joseph (FNIH) [T] < (b) (6) : Adam, Stacey (FNIH) [T] (b) (6)
Wholley, David (FNIH) [T] (b) (6)
Subject: Slides for Hever Antiviral Meeting

Hi Francis,

Attached are draft slides for the Hever Antiviral meeting this week. Joe and Stacey have provided updates and standby if any additional information is needed.

Thanks,
Ashley

From: Menetski, Joseph (FNIH) [T] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=5001AF52DC4A427EA3D34F1E072F8CB7-MENETSKIJP]
Sent: 8/28/2020 3:39:38 PM
To: Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]
CC: Elsaid, Olivia [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=userf0efa7bd]; Gonzalez, Nina [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=user3c2f486d]; Appell, Evan [(b) (6) Adam, Stacey (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dcd875f0679648859e1cf101c0943414-adamsj4]
Subject: RE: ACTIV LT Prioritization Slide

Ashley,
I am glad to hear that Francis is talking at Hever about this. We would actually like him (and Dr. Dolsten) to encourage the members to submit any antivirals they might be interested in progressing through the ACTIV survey that the preclinical and clinical group have been using.

I am not sure we want to provide the names of those assets that have been deferred as that may lead to members second guessing the expert panels that we have working this (in both the clinical and preclinical space) and undermine their credibility.

I think that Stacey and I can put together a list of all the antivirals that we have evaluated in depth and the number of those hat started the process. Which have been suggested to trials and those that have been suggested to further preclinical testing? Would that be helpful?

Joe

From: Wholley, David (FNIH) [T] < (b) (6)
Sent: Friday, August 28, 2020 11:32 AM
To: Parker, Ashley (NIH/OD) [E] < (b) (6) Menetski, Joseph (FNIH) [T] < (b) (6)
Cc: Elsaid, Olivia < (b) (6) Gonzalez, Nina < (b) (6) Appell, Evan < (b) (6) Adam, Stacey (FNIH) [T] < (b) (6)
Subject: RE: ACTIV LT Prioritization Slide

Keeping Stacey in the loop. Antivirals are part of both the preclinical and clinical WG discussions.

From: Parker, Ashley (NIH/OD) [E] (b) (6)
Sent: Friday, August 28, 2020 11:32 AM
To: Menetski, Joseph (FNIH) [T] < (b) (6) Wholley, David (FNIH) [T] < (b) (6)
Cc: Elsaid, Olivia (b) (6) Gonzalez, Nina (b) (6) ; Appell, Evan (b) (6)
Subject: RE: ACTIV LT Prioritization Slide

Hi Joe,

Yes, Francis is presenting this to the Hever group for their antiviral meeting on Wed. They will likely want to see the antivirals that were deferred, assuming there are 3 antivirals deferred

Can we please have a updated version unless you recommend he not share those antivirals that were deferred? I planned to remove the other compounds (immune modulators and other therapies) not pertinent to the discussion unless suggested otherwise.

Thanks,
Ashley

From: Menetski, Joseph (FNIH) [T] (b) (6)
Sent: Friday, August 28, 2020 11:24 AM
To: Parker, Ashley (NIH/OD) [E] < (b) (6) Wholley, David (FNIH) [T] (b) (6)
Cc: Elsaid, Olivia (b) (6) >; Gonzalez, Nina (b) (6) Appell, Evan (b) (6)
Subject: RE: ACTIV LT Prioritization Slide

Ashley,

The ones that were deferred from evaluation, mostly because they were too early, were not listed in the box. Only the ones in the box were evaluated in depth.

If that is not clear, please don't hesitate to contact me.

Joe

From: Parker, Ashley (NIH/OD) [E] < (b) (6)
Sent: Friday, August 28, 2020 11:21 AM
To: Wholley, David (FNIH) [T] (b) (6)
Cc: Menetski, Joseph (FNIH) [T] (b) (6) Elsaid, Olivia (b) (6) Gonzalez, Nina (b) (6) Appell, Evan (b) (6)
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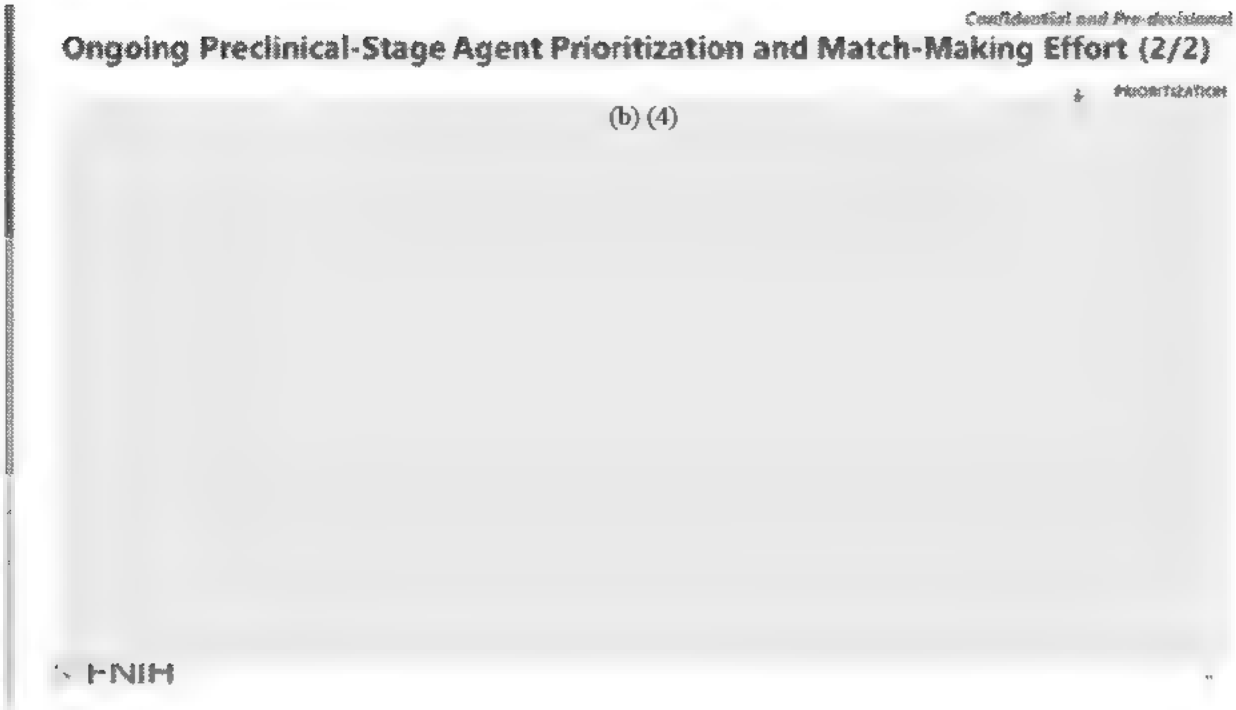
Hi David,

Per our discussion on the war room call this morning, I am pulling the antiviral data from the slides presented to the LT meeting on Wed. and noticed the number of antivirals in the wave 1 prioritization do not match the number of agents listed, please see below (7 antivirals with 4 antiviral agents listed).

This may have been corrected on the version displayed to the LT – could I please have a copy of the revised version?



Thanks,
Ashley

Ashley Parker, Ph.D.
Special Assistant to the NIH Director for Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)
Office of the Director | National Institutes of Health
Tel: (b) (6)
National Institutes of Health

From: Adam, Stacey (FNIH) [T] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=DCD875F0679648859E1CF101C0943414-ADAMSJ4]
Sent: 8/28/2020 3:37:52 PM
To: Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]; Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Menetski, Joseph (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5001af52dc4a427ea3d34f1e072f8cb7-menetskijp]
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Subject: RE: ACTIV LT Prioritization Slide

Thanks, Ashley,

Thank you for this then. You can ignore my query in the last email then.

Thanks,
Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: (b) (6) Mobile: (b) (6)

From: Parker, Ashley (NIH/OD) [E] < (b) (6)
Sent: Friday, August 28, 2020 11:34 AM
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Subject: RE: ACTIV LT Prioritization Slide

Yes, thanks – had not made it to clinical antiviral slides yet!

Thanks!!
Ashley

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Sent: Friday, August 28, 2020 11:32 AM
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Cc: Elsaid, Olivia (b) (6) >; Gonzalez, Nina < (b) (6) Appell, Evan (b) (6) ; Adam, Stacey (FNIH) [T] <; (b) (6)
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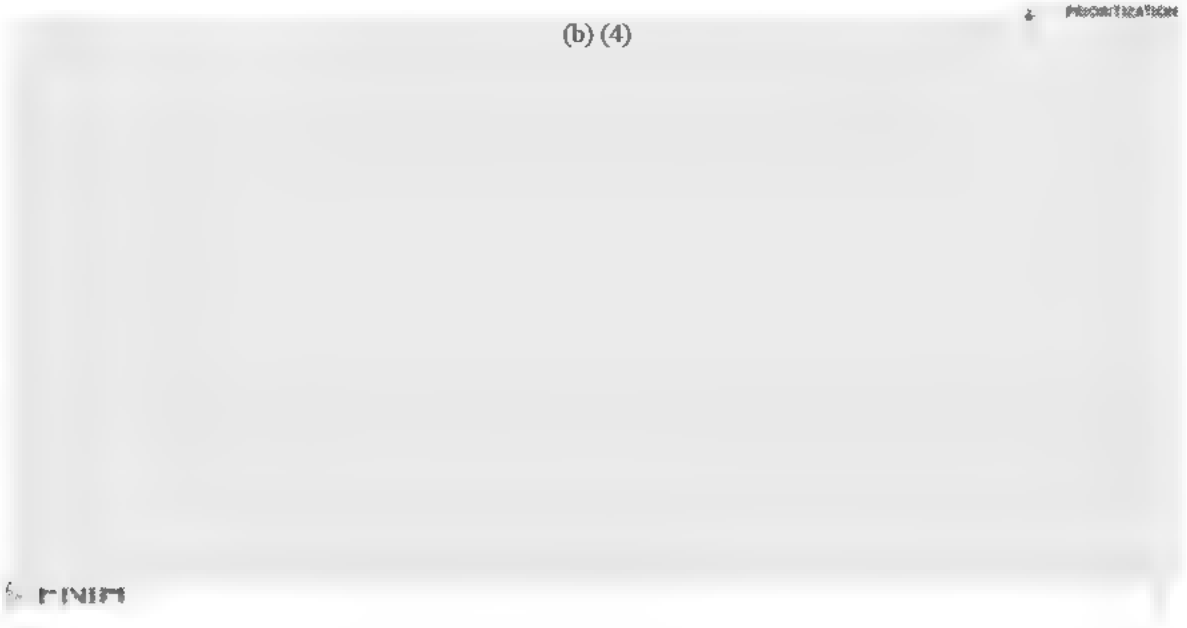
Confidential and Pre-decisional

Ongoing Preclinical-Stage Agent Prioritization and Match-Making Effort (2/2)

(b) (4)



Thanks,
Ashley

Ashley Parker, Ph.D.
Special Assistant to the NIH Director for Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)
Office of the Director | National Institutes of Health
Tel: (b) (6)
National Institutes of Health

From: Adam, Stacey (FNIH) [T] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=DCD875F0679648859E1CF101C0943414-ADAMSJ4]
Sent: 9/2/2020 12:07:37 PM
To: Menetski, Joseph (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5001af52dc4a427ea3d34f1e072f8cb7-menetskijp]; Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]; Freire, Mar a (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Austin, Christopher (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=17597cabc42247548e596778304f781f-austinc]; Lane, Cliff (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]; Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]
Subject: RE: Hever COVID-19 Antivirals Meeting Sept 2 SLIDES AND MATERIAL

Hi Everyone,

I agree with Joe. I think we should be very hesitant to provide these reviews to anyone outside the ACTIV program/USG. At least the longer reviews, we do provide the short one line explanation to the submitter when we let them know their compound was not selected, so that could likely be provided to external groups. However, the longer detailed reviews from the ACTIV reviewers should I believe remain confidential.

Thanks,
Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: (b) (6) | Mobile: (b) (6)

From: Menetski, Joseph (FNIH) [T] < (b) (6)
Sent: Wednesday, September 2, 2020 7:54 AM
To: Collins, Francis (NIH/OD) [E] < (b) (6) Freire, Maria (FNIH) [T] < (b) (6) Wholley, David (FNIH) [T] < (b) (6) Tabak, Lawrence (NIH/OD) [E] < (b) (6) Austin, Christopher (NIH/NCATS) [E] < (b) (6) Lane, Cliff (NIH/NIAID) [E] < (b) (6) Parker, Ashley (N H/OD) [E] < (b) (6) Anderson, James (NIH/OD) [E] < (b) (6) Adam, Stacey (FNIH) [T] < (b) (6)
Subject: RE: Hever COVID-19 Antivirals Meeting Sept 2 SLIDES AND MATERIAL

Last question first, the antivirals (and other therapeutics) ultimately were submitted through the survey. Some were encourage from the LT and others, others came as a result of first submitting to the NIH portal.

I will let Stacey answer the decision question, but we do have extensive feedback on almost all of these compounds (unless if it was triaged out of the process quickly. Example, hydrogenated water). There are also short answer reasons

for deferring. My opinion is that these reviews are like an NIH grant reviews and we should be hesitant to provide detailed information in a broad way.

With respect to the compendium, this is a small subset of everything out there, no surprises that I see, except some are not antivirals.

I like the new co idea, but wonder how much interest there will be in funding, after we get a handle on COVID.

From: Collins, Francis (NIH/OD) [E] (b) (6)
Sent: Wednesday, September 2, 2020 7:40 AM
To: Freire, Maria (FNIH) [T] < (b) (6) Wholley, David (FNIH) [T] < (b) (6) Tabak, Lawrence (NIH/OD) [E] (b) (6) ; Austin, Christopher (NIH/NCATS) [E] (b) (6) ; Lane, Cliff (NIH/NIAID) [E] (b) (6) Parker, Ashley (NIH/OD) [E] (b) (6) ; Anderson, James (NIH/OD) [E] < (b) (6) Menetski, Joseph (FNIH) [T] < (b) (6) Adam, Stacey (FNIH) [T] (b) (6)
Subject: RE: Hever COVID-19 Antivirals Meeting Sept 2 SLIDES AND MATERIAL

One more question will get asked – what was the input mechanism for ACTIV's list of potential antivirals?

From: Collins, Francis (NIH/OD) [E]
Sent: Wednesday, September 2, 2020 7:06 AM
To: Freire, Maria (FNIH) [T] (b) (6) Wholley, David (FNIH) [T] (b) (6) Tabak, Lawrence (NIH/OD) [E] (b) (6) Austin, Christopher (NIH/NCATS) [E] (b) (6) ; Lane, Cliff (NIH/NIAID) [E] (b) (6) >; Parker, Ashley (NIH/OD) [E] (b) (6) >; Anderson, James (NIH/OD) [E] < (b) (6) Menetski, Joseph (FNIH) [T] (b) (6) Adam, Stacey (FNIH) [T] (b) (6)
Subject: FW: Hever COVID-19 Antivirals Meeting Sept 2 SLIDES AND MATERIAL

Hi all,

Please see the attached slide sets for this morning's Hever meeting on antivirals. We can discuss at the 8 AM War Room call.

I am pretty sure I will be asked whether ACTIV is willing to share materials that led to decisions about Go/Defer/No in Waves 1 – 3. Is there a file on each compound that was considered, and are we willing to provide that to interested parties?

Please check out the second attachment – does this compendium of antivirals contain any surprises?

Please look at Andy Plump's proposal about a NewCo for developing therapeutics in future pandemics. Does that make sense to you?

If I could get feedback (especially from Stacey and Joe) by 11 AM, that would be great!

Francis

From (b) (6)
Sent: Tuesday, September 1, 2020 11:00 PM
Cc: (b) (6) >; Trevor Jones < (b) (6) (b) (6) Geoff Frew (b) (6) (b) (6)

(b) (6) (b) (6)

< (b) (6)

Subject: Hever COVID-19 Antivirals Meeting Sept 2 SLIDES AND MATERIAL

Dear All,

Please find enclosed

1) A master deck with presentation slides for tomorrow
2) An excel table with overview of compounds considered for the NIH ACTIV Antivirals Trial
3) COVID-19 antivirals small molecule overview slide deck

Please, note that Dr. Bradner's presentation Is not included in the circulated master deck as it was too big to send by e-mail. It alongside comprehensive background information will be circulated separately via a link..
For tomorrow we should be able however to run all slides from a single computer.

Looking forward to a good discussion.

Best Regards on behalf of Trevor and (b) (6)

(b) (6)

From: Adam, Stacey (FNIH) [T] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=DCD875F0679648859E1CF101C0943414-ADAMSJ4]
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Subject: RE: ACTIV LT Prioritization Slide

Thanks, David,

The slide disp ayed was only the preclinical antiviral compounds are we discussing the ones in consideration for clinical trials? If so, we wil need another slide.

Thanks,
Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: (b) (6) | Mobile: (b) (6)

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Cc: Elsaid, Olivia < (b) (6) Gonzalez, Nina < (b) (6) Appell, Evan < (b) (6) Adam, Stacey (FNIH) [T] < (b) (6)
Subject: RE: ACTIV LT Prioritization Slide

Keeping Stacey in the loop. Antivirals are part of both the preclinical and clinical WG discussions.

From: Parker, Ashley (NIH/OD) [E] (b) (6)
Sent: Friday, August 28, 2020 11:32 AM
To: Menetski, Joseph (FNIH) [T] (b) (6) Wholley, David (FNIH) [T] (b) (6)
Cc: Elsaid, Olivia (b) (6) . Gonzalez, Nina (b) (6) ; Appell, Evan < (b) (6)
Subject: RE: ACTIV LT Prioritization Slide

Hi Joe,

Yes, Francis is presenting this to the Hever group for their antiviral meeting on Wed. They will likely want to see the antivirals that were deferred, assuming there are 3 antivirals deferred.

Can we please have a updated version unless you recommend he not share those antivirals that were deferred? I planned to remove the other compounds (immune modulators and other therapies) not pertinent to the discussion unless suggested otherwise.

Thanks,
Ashley

From: Menetski, Joseph (FNIH) [T] (b) (6)
Sent: Friday, August 28, 2020 11:24 AM
To: Parker, Ashley (NIH/OD) [E] < (b) (6) Wholley, David (FNIH) [T] (b) (6) >
Cc: Elsaid, Olivia (b) (6) Gonzalez, Nina (b) (6) Appell, Evan (b) (6)
Subject: RE: ACTIV LT Prioritization Slide

Ashley,

The ones that were deferred from evaluation, mostly because they were too early, were not listed in the box. Only the ones in the box were evaluated in depth.

If that is not clear, please don't hesitate to contact me.

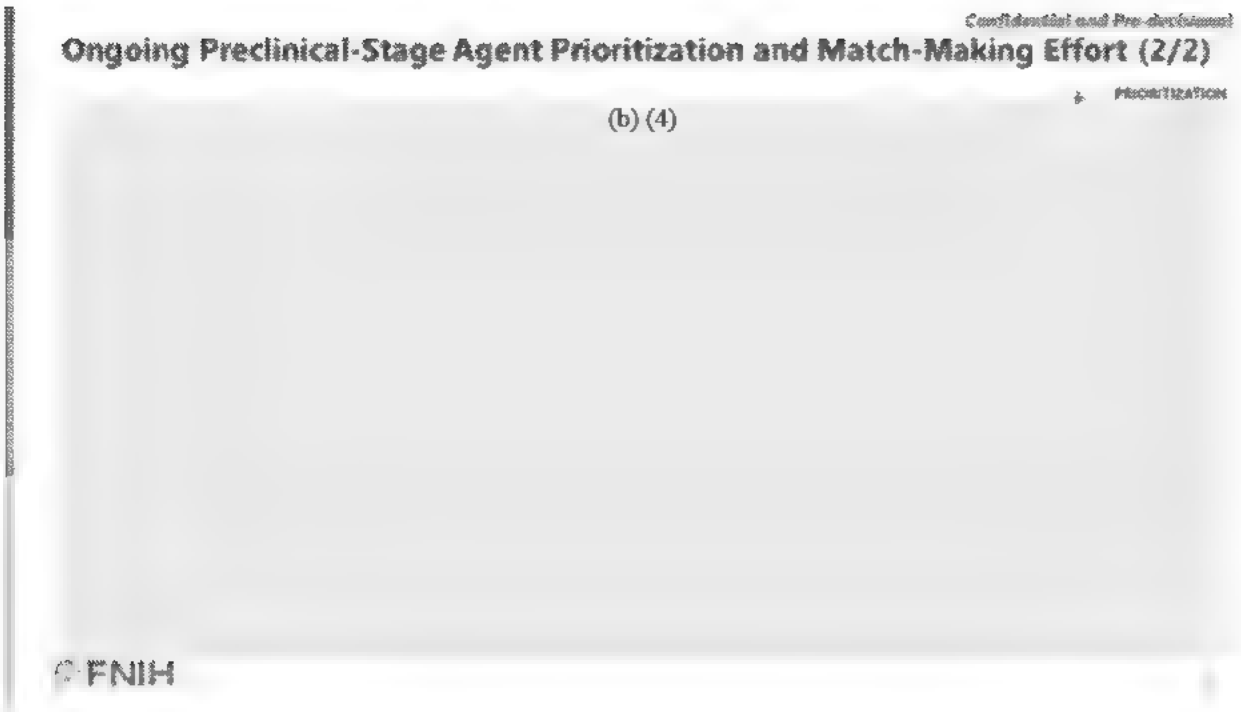
Joe

From: Parker, Ashley (NIH/OD) [E] < (b) (6)
Sent: Friday, August 28, 2020 11:21 AM
To: Wholley, David (FNIH) [T] < (b) (6)
Cc: Menetski, Joseph (FNIH) [T] < (b) (6) Elsaid, Olivia (b) (6) Gonzalez, Nina (b) (6) Appell, Evan < (b) (6)
Subject: ACTIV LT Prioritization Slide

Hi David,

Per our discussion on the war room call this morning, I am pulling the antiviral data from the slides presented to the LT meeting on Wed. and noticed the number of antivirals in the wave 1 prioritization do not match the number of agents listed, please see below (7 antivirals with 4 antiviral agents listed)

This may have been corrected on the version displayed to the LT – could I please have a copy of the revised version?



Thanks,
Ashley

Ashley Parker, Ph.D.
Special Assistant to the NIH Director for Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV)
Office of the Director | National Institutes of Health
Tel: (b) (6)
National Institutes of Health

From: Adam, Stacey (FNIH) [T] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=DCD875F0679648859E1CF101C0943414-ADAMSJ4]
Sent: 9/2/2020 12:03:26 PM
To: Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]; Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]; Freire, Mar a (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]; Austin, Christopher (NIH/NCATS) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=17597cabc42247548e596778304f781f-austinc]; Lane, Cliff (NIH/NIAID) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=2d7e368a3137473bbce161547a82f2de-clane]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]; Anderson, James (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=73143d1860bc42458be254ca21573b23-andersonjm]; Menetski, Joseph (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5001af52dc4a427ea3d34f1e072f8cb7-menetskijp]
Subject: RE: Hever COVID-19 Antivirals Meeting Sept 2 SLIDES AND MATERIAL

Hi David,

Those are the only two sources for now, with the public sources mostly being used for Wave 1 and the survey responses for Wave 2 and 3.

Thanks,
Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: (b) (6) | Mobile: (b) (6)

From: Wholley, David (FNIH) [T] < (b) (6)
Sent: Wednesday, September 2, 2020 7:48 AM
To: Collins, Francis (NIH/OD) [E] < (b) (6) Freire, Maria (FNIH) [T] < (b) (6) Tabak, Lawrence (NIH/OD) [E] < (b) (6) Austin, Christopher (NIH/NCATS) [E] < (b) (6) Lane, Cliff (NIH/NIAID) [E] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6) Anderson, James (NIH/OD) [E] < (b) (6) Menetski, Joseph (FNIH) [T] < (b) (6) Adam, Stacey (FNIH) [T] < (b) (6)
Subject: RE: Hever COVID-19 Antivirals Meeting Sept 2 SLIDES AND MATERIAL

Public databases and compound survey responses. Any others, Stacey?

From: Collins, Francis (NIH/OD) [E] (b) (6)
Sent: Wednesday, September 2, 2020 7:40 AM
To: Freire, Maria (FNIH) [T] < (b) (6) Wholley, David (FNIH) [T] < (b) (6) Tabak, Lawrence (NIH/OD) [E] (b) (6) >; Austin, Christopher (NIH/NCATS) [E] (b) (6) Lane, Cliff (NIH/NIAID) [E] < (b) (6) Parker, Ashley (NIH/OD) [E] <; (b) (6) Anderson, James

(NIH/OD) [E] < (b) (6) Menetski, Joseph (FNIH) [T] < (b) (6) Adam, Stacey (FNIH) [T] < (b) (6)
Subject: RE: Hever COVID-19 Antivirals Meeting Sept 2 SLIDES AND MATERIAL

One more question will get asked what was the input mechanism for ACTIV's list of potential antivirals?

From: Collins, Francis (NIH/OD) [E]
Sent: Wednesday, September 2, 2020 7:06 AM
To: Freire, Maria (FNIH) [T] (b) (6) Wholley, David (FNIH) [T] (b) (6) Tabak, Lawrence (NIH/OD) [E] (b) (6) ; Austin, Christopher (NIH/NCATS) [E] (b) (6) Lane, Cliff (NIH/NIAID) [E] (b) (6) ; Parker, Ashley (NIH/OD) [E] (b) (6) Anderson, James (NIH/OD) [E] < (b) (6) Menetski, Joseph (FNIH) [T] (b) (6) Adam, Stacey (FNIH) [T] < (b) (6)
Subject: FW: Hever COVID-19 Antivirals Meeting Sept 2 SLIDES AND MATERIAL

Hi all,

Please see the attached slide sets for this morning's Hever meeting on antivirals. We can discuss at the 8 AM War Room call.

I am pretty sure I will be asked whether ACTIV is willing to share materials that led to decisions about Go/Defer/No in Waves 1 – 3. Is there a file on each compound that was considered, and are we willing to provide that to interested parties?

Please check out the second attachment – does this compendium of antivirals contain any surprises?

Please look at Andy Plump's proposal about a NewCo for developing therapeutics in future pandemics. Does that make sense to you?

If I could get feedback (especially from Stacey and Joe) by 11 AM, that would be great!

Francis

From: (b) (6)
Sent: Tuesday, September 1, 2020 11:00 PM
Cc: (b) (6) ; Trevor Jones (b) (6) (b) (6) ; Geoff Frew (b) (6) >; (b) (6) (b) (6) (b) (6) (b) (6)

Subject: Hever COVID-19 Antivirals Meeting Sept 2 SLIDES AND MATERIAL

Dear All,

Please find enclosed

1) A master deck with presentation slides for tomorrow
2) An excel table with overview of compounds considered for the NIH ACTIV Antivirals Trial
3) COVID-19 antivirals small molecule overview slide deck

Please, note that Dr. Bradner's presentation Is not included in the circulated master deck as it was too big to send by e-mail. It alongside comprehensive background information will be circulated separately via a link..

For tomorrow we should be able however to run all slides from a single computer.

Looking forward to a good discussion.

Best Regards on behalf of Trevor and (b) (6)

(b) (6)

From: Myles, Renate (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=7D317F5626934585B3692A1823C1B522-MYLESR]
Sent: 5/20/2020 1:00:53 PM
To: Melencio, Cheryl (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=279e14fa7428415bb86087d08b628e6f-melencioc]; Meltzer, Abbey (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=c341d86cf7404a78ac8f852e698e5382-meltzerak], Gorman, Greta (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=280703da933d491586841696e460f062-gormanmj]
CC: Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]
Subject: RE: Notes from the Vaccines WG meeting; Animal Model request; WG/SG member names to be made available

Hi Cheryl:

These updates are made. Let me know if/when you hear from others.

Just a note that Francis asked that I add BMGF to the list of Non-Profit Leadership Organizations, which was added. Just wanted to make sure you, Abbey and Greta are aware. I also understand we're adding a few more folks to the EC. Ashley will provide me with those names and organizations and we'll update it today.

Thanks,
Renate

From: Melencio, Cheryl (FNIH) [T] < (b) (6)
Sent: Tuesday, May 19, 2020 3:38 PM
To: Myles, Renate (NIH/OD) [E] < (b) (6) Meltzer, Abbey (FNIH) [T] < (b) (6) Gorman, Greta (FNIH) [T] < (b) (6)
Cc: Parker, Ashley (NIH/OD) [E] < (b) (6)
Subject: FW: Notes from the Vaccines WG meeting; Animal Model request; WG/SG member names to be made available

See below – please use this:
Beth Bell, M.D.
Clinical Professor, Global Health
University of Washington

Cheryl Melencio
Administrative Manager, Research Partnerships
Foundation for the National Institutes of Health
(b) (6)
fnih.org
11400 Rockville Pike Suite 600 North Bethesda, MD 20852

From: Beth Bell (b) (6)
Sent: Tuesday, May 19, 2020 3:25 PM
To: Melendio, Cheryl (FNIH) [T] (b) (6)
Subject: Fwd: Notes from the Vaccines WG meeting, Animal Model request; WG/SG member names to be made available

See below, as noted.

Sent from my iPad

Begin forwarded message:

> **From:** Beth Bell (b) (6)
> **Date:** May 13, 2020 at 6:36:18 AM PDT
> **To:** "Santos, Michael (FNIH) [T]" (b) (6)
> **Subject: Re: Notes from the Vaccines WG meeting; Animal Model request; WG/SG member names to be made available**
>
> Michael,
>
> I am not sure it's wise to describe me publicly as a former director of NCEZID at CDC. Maybe good for awareness of other WG members, but not appropriate publicly. So best to keep to my UW clinical appointment.
> Many thanks for all the excellent work.
>
> Beth Bell
>
> Sent from my iPad
>
> > On May 12, 2020, at 3:26 PM, Santos, Michael (FNIH) [T] (b) (6) wrote:
> >
> > Dear Vaccines Working Group members (and cc'ing others for awareness),
> >
> > Thank you for your participation in yesterday's meeting. Attached are the summary notes from the meeting, plus an updated copy of the previous meeting's notes correcting two attendance omissions. Attached are also updated notes from the last meeting of the Protective Immune Responses Sub-Group, with updates to the content based on input from meeting participants. As always, please send any feedback on meeting notes and we will be happy to update and recirculate.
> >
> > The Preclinical Working Group is collecting an animal model inventory. They have invited us to provide input on the **columns** of the attached spreadsheet, particularly the 'NHPs' tab: i.e., the request is for **what information they should collect in their inventory**, *not* to attempt to provide an inventory. We will ask the Protective Immune Responses Sub-Group to review, but are making the spreadsheet available to the whole group as anyone is invited to provide input by the end of this week. For awareness, the most recent Preclinical WG notes are also attached.

Finally, we have been informed that **the NIH intends to make the names of ACTIV Working Group and Sub-Group members publicly available** in the near future. Please contact us if you have any questions or concerns.

Best regards,
Brett and Mike

Michael Santos, PhD
Associate Vice President, Science | Foundation for the National Institutes of Health

From: Santos, Michael (FNIH) [T]
Sent: Saturday, May 9, 2020 10:16 PM
Subject: Review requested: Human Challenge Model draft; notes from Vaccines Sub-Groups, ACTIV Leadership Team, and Preclinical WG

Dear Vaccines Working Group members (and cc'ing others for awareness),

This note is an omnibus update for the Working Group: Sub-Group meeting notes, the human challenge model draft and agenda for the Working Group meeting, upcoming Vaccines Clinical Trial Sub-Group meetings and topics, and for awareness notes from the ACTIV Leadership Team meeting and Preclinical WG.

Sub-Group meeting notes
As a reminder, the Protective Immune Responses and Vaccine-associated Immune Enhancement Sub-Groups met since our last Working Group meeting (Thurs and Fri, respectively). Thank you to all who participated or sent input. **Attached are the notes and action items from each meeting**. The agendas and meeting materials and pre-reads are embedded in those documents. If anyone would like to be added to the lists for either Sub-Group, please let us know.

Review Controlled Human Infection Model outline in preparation for Monday's Working Group meeting
The main agenda item at the next Vaccines Working Group meeting, Monday, 12pm ET (9am PT / 6pm CEST), is a discussion of the Working Group's perspective on a CoV-2 controlled human infection model. Please review the attached outline to prepare for that discussion. If you cannot attend the meeting, feel free to send input via email that we can represent

Vaccines Clinical Trial Sub-Group updates
Members of this Sub-Group are invited on Tuesday (11am ET) to join the Clinical Trial Capacity Working Group meeting, where Paula and Larry will share the plans of the Sub-Group and the CTC WG will share their activities and how they can work with us (e.g., inventory trial site capacity). **The Sub-Group meeting Wednesday (1pm ET) will focus on key protocol questions.**

ACTIV Leadership Team meeting notes
Last Wednesday, the ACTIV Leadership Team (the parent body above the Working Groups) met. Kathrin and Doug presented the progress and plans of the Working Group and answered questions. The meeting presentation and notes are attached. **Note: This is a good way to see a high-level summary of the activities of the other Working Groups, many of which are relevant to our work**, if you have specific questions, let us know and we can follow up.

Pre-clinical Working Group
Finally, as discussed last week we will continue to share notes from the Preclinical Working Group for awareness (attached zip file). **Note: a request to review the data collection fields for animal models will be coming to our group**, which we will circulate to the Protective Immune Responses and Vaccine-associated Immune Enhancement Sub-Groups.

As always, please don't hesitate to reach out with any questions or suggestions.

Best regards,
Brett and Mike

Michael Santos, PhD
Associate Vice President, Science
Foundation for the National Institutes of Health
(b) (6) fnih.org
11400 Rockville Pike, Suite 600, North Bethesda, MD 20852

Stay at the forefront of FNIH news: fnih.org/newsletter

<2020-05-11 Working Group meeting Summary Notes.docx>
<2020-05-05 Working Group meeting Summary Notes-updated.docx>
<2020-05-07 Protective Immune Responses Sub-Group meeting Notes-updated.docx>
<ACTIV PRECLINICAL_Animal Model Inventory_20200507.xlsx>
<2020-05-08_Preclinical_WG_Summary_D3.docx>

From: Collins, Francis (NIH/OD) [E] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=410E1CA313F44CED9938E50D2FF0B6C2-COLLINSF]
Sent: 3/2/2021 10:33:40 PM
To: Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]
CC: Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]; Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]; Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]
Subject: RE: MEDI3506_Covid-19

Yes, thanks.

From: Wholley, David (FNIH) [T] < (b) (6)
Sent: Tuesday, March 2, 2021 3:24 PM
To: Collins, Francis (NIH/OD) [E] < (b) (6)
Cc: Freire, Maria (FNIH) [T] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6) Tabak, Lawrence (NIH/OD) [E] < (b) (6)
Subject: RE: MEDI3506_Covid-19

OK, want me to respond?

From: Collins, Francis (NIH/OD) [E] (b) (6)
Sent: Tuesday, March 2, 2021 2:50 PM
To: Wholley, David (FNIH) [T] (b) (6)
Cc: Freire, Maria (FNIH) [T] (b) (6) Parker, Ashley (NIH/OD) [E] (b) (6) >; Tabak, Lawrence (NIH/OD) [E] < (b) (6)
Subject: RE: MEDI3506_Covid-19

I didn't see anything in Hitesh's note to suggest preliminary data on efficacy – he says they are about to finish recruiting 60 hospitalized patients. It will be at least a month or two before they know the results of that. So this doesn't sound like an "extraordinary opportunity" to me.

FC

From: Wholley, David (FNIH) [T] (b) (6) >
Sent: Tuesday, March 2, 2021 10:34 AM
To: Collins, Francis (NIH/OD) [E] (b) (6)
Cc: Freire, Maria (FNIH) [T] < (b) (6) Parker, Ashley (NIH/OD) [E] (b) (6) >; Tabak, Lawrence (NIH/OD) [E] (b) (6)
Subject: FW: MEDI3506_Covid-19

Francis:
I'm not sure we can accommodate Hitesh's request at this time. ACTIV-1 simply does not have the capacity to test other agents—there are challenges just to have them complete testing with the agents they have, and we know NCATS will be busy also taking on ACTIV-6. We are of course already testing an anti-inflammatory mAb in ACTIV-5 (albeit an IL-23, Risankizumab) so it's not like this is a completely new class of therapeutic for us. I doubt this agent rises to the level of the kind of "extraordinary opportunity" we discussed in yesterday's war room that would cause us to ca l back the prioritization team and have them comb through all the ACCORD data to evaluate this drug, only for us to have to say

we have no existing trial to put it in—and, of course, no money to fund the study. We could possibly refer him to Sarah and Eric for the sake of politesse, but I prefer we just say no right now. Thoughts?

David

From: Pandya, Hitesh (b) (6)
Sent: Tuesday, March 2, 2021 8:13 AM
To: Wholley, David (FNIH) [T] (b) (6) Collins, Francis (NIH/OD) [E] (b) (6)
Subject: MEDI3506_Covid-19

Dear David and Francis,

I hope you are both well.

As a Medical Science Director at AZ (and a 'lapsed' paediatric and ECMO intensivist in UK NHS), my apologies for not being more engaged in the FNIH Covid-19 initiative. I have been very much involved in UK Covid-19 platform called ACCORD, that has absorbed much of my time.

One of the AZ assets in ACCORD, MEDI3506 (an anti-IL-33 mAb), is close to completing recruitment (n=60 per arm, MEDI3506 vs SoC open label). ACCORD is designed to assess safety of early phase assets in Covid -19 (hospitalized patents) and, hopefully, provide an early signal on efficacy. Hence, I have thinking about potential next steps for this potential medicine and, so, I am reaching out about feasibility and opportunity to include MEDI3506 in ACTIV-1.

I would be happy to arrange an off-line meeting, if that is a suitable way forward, at least initially.

Kind regards

Hitesh

Hitesh Pandya, MB.Ch.B (Glasgow), MRCP (UK), MD (Kings College, London), FHEA (UK)
Physician, Medical Science Director
Early Respiratory & Immunology
BioPharmaceuticals R&D,
AstraZeneca
(b) (6)

From: Freire, Maria (FNIH) [T] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=8598D551D1D3455EAF14854C83F41D84-FREIREMC]
Sent: 3/2/2021 8:15:54 PM
To: Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]; Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]
CC: Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]; Tabak, Lawrence (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=02e22836b5ff4e9988e3770cfc7ee770-tabakl]
Subject: RE: MEDI3506_Covid-19

Francis I am starting to worry about the long-term commitment of some companies to ID. This is not entirely surprising given that for most th s type of disease in not their core business. Their best shot is to get the USG to pick up the tab. That way they are off the hook. I cannot really blame them, this was predictable. It is VERY unfortunate, though. M.

From: Collins, Francis (NIH/OD) [E] < (b) (6)
Sent: Tuesday, March 2, 2021 2:50 PM
To: Wholley, David (FNIH) [T] < (b) (6)
Cc: Freire, Maria (FNIH) [T] < (b) (6) Parker, Ashley (NIH/OD) [E] < (b) (6) Tabak, Lawrence (NIH/OD) [E] < (b) (6)
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David

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Sent: Tuesday, March 2, 2021 8:13 AM
To: Wholley, David (FNIH) [T] <g (b) (6) Collins, Francis (NIH/OD) [E] (b) (6)
Subject: MEDI3506_Covid-19

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Kind regards

Hitesh

Hitesh Pandya, MB.Ch.B (Glasgow), MRCP (UK), MD (Kings College, London), FHEA (UK)
Physician, Medical Science Director
Early Respiratory & Immunology
BioPharmaceuticals R&D,
AstraZeneca
(b) (6)

From: Menetski, Joseph (FNIH) [T] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=5001AF52DC4A427EA3D34F1E072F8CB7-MENETSKIJP]
Sent: 1/3/2021 9:58:01 PM
To: Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]; Freire, Maria (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=8598d551d1d3455eaf14854c83f41d84-freiremc]
CC: Wholley, David (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cd9e702fcf28414883d0b6996d677257-wholleyd]
Subject: RE: Mutation tracking plan is not dead yet

Karl Erlandson. He has been involved in the OWS preclinical group too.

joe

From: Collins, Francis (NIH/OD) [E] < (b) (6)
Sent: Sunday, January 3, 2021 4:52 PM
To: Menetski, Joseph (FNIH) [T] < (b) (6) Freire, Maria (FNIH) [T] < (b) (6)
Cc: Wholley, David (FNIH) [T] < (b) (6)
Subject: RE: Mutation tracking plan is not dead yet

Just so I know, who from BARDA had a look at the plan and had a chance to provide input?

From: Menetski, Joseph (FNIH) [T] < (b) (6)
Sent: Sunday, January 3, 2021 4:11 PM
To: Collins, Francis (NIH/OD) [E] (b) (6) Freire, Maria (FNIH) [T] (b) (6)
Cc: Wholley, David (FNIH) [T] (b) (6)
Subject: RE: Mutation tracking plan is not dead yet

Hi Francis,

Here is the proposal covering 50 variants for 1 year [$18, 375,00].

I wanted to let you know that while the immediate authors of the proposal did not include BARDA, we took the information from to overall subgroup which had a lot of input from BARDA and CDC. The proposal has been shared with the subgroup and BARDA has had a chance to provide input (althought not at the level of Gary Disbrow).

I will keep checking my email incase you need any additional information or there is a question about the proposal.

Best regards,
Joe

From: Collins, Francis (NIH/OD) [E] (b) (6)
Sent: Sunday, January 3, 2021 10:30 AM
To: Freire, Maria (FNIH) [T] (b) (6) >
Cc: Menetski, Joseph (FNIH) [T] (b) (6) Wholley, David (FNIH) [T] (b) (6) >
Subject: RE: Mutation tracking plan is not dead yet

Hi Maria,

I haven't heard back from Joe, so perhaps he is taking a break but it would be great to have new version by the end of today, so that I could start pitching it to CDC and BARDA. I don't think it will take Joe very long to do this.

Thanks, Francis

From: Freire, Maria (FNIH) [T] < (b) (6)
Sent: Saturday, January 2, 2021 11:38 AM
To: Collins, Francis (NIH/OD) [E] < (b) (6) >
Cc: Menetski, Joseph (FNIH) [T] (b) (6) ; Wholley, David (FNIH) [T] (b) (6)
Subject: Re: Mutation tracking plan is not dead yet

Happy New Year, Francis!

Well, we can't blame Moncef for being sensitive to the limited timeframe. I know Joe can put the numbers together rather quickly. I am not sure he is online right now - when do you want to send them so I can call him if need be? M.

From: "Collins, Francis (NIH/OD) [E]" (b) (6)
Date: Saturday, January 2, 2021 at 11:25:02 AM
To: "Menetski, Joseph (FNIH) [T]" (b) (6)
Cc: "Wholley, David (FNIH) [T]" (b) (6) "Freire, Maria (FNIH) [T]" (b) (6) >, "Anderson, James (NIH/OD) [E]" (b) (6) , "Austin, Christopher (NIH/NCATS) [E]" (b) (6) >, "Tabak, Lawrence (NIH/OD) [E]" (b) (6) "Patterson, Amy (NIH/NHLBI) [E]" (b) (6) "Lane, Cliff (NIH/NIAID) [E]" (b) (6) >, "Parker, Ashley (NIH/OD) [E]" (b) (6)
Subject: Mutation tracking plan is not dead yet

Hi Joe,

I spoke with Moncef about the mutation tracking program. He filled me in a bit more on the discussion that was he d about our proposal. It seems they were skittish about making this kind of longer term commitment (3 years, $90M), when the new administration will be here in 18 days. They were also seeing this as being driven by N H, rather than considering my advocacy as reflective of my role as co-chair of the ACTIV Executive Committee. They were concerned that CDC might not be fully supportive, and that BARDA hadn't really been involved.

The good news is that Moncef is personally quite supportive. He suggests reworking this as a one-year proposal, and then getting support at higher levels of CDC (Nancy Messonnier and/or Anne Schuchat) and from BARDA (Gary Disbrow and Robert Johnson). If they signal support, then Moncef thought he could push this through the OWS budgetary process fairly quickly.

Can you do a quick revision to focus on one year and 50 variant viral genomes? Then I'll work on marketing to CDC and BARDA.

I think we have a good chance here. Paul Stoffels is also prepared to advocate for this program if needed.

Francis

From: Freire, Maria (FNIH) [T] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=8598D551D1D3455EAF14854C83F41D84-FREIREMC]
Sent: 9/2/2020 11:48:47 AM
To: Collins, Francis (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=410e1ca313f44ced9938e50d2ff0b6c2-collinsf]
Subject: Re: Hever COVID-19 Antivirals Meeting Sept 2 SLIDES AND MATERIAL

Francis, just for you.

I have only skimmed Andy's proposal on the NewCo. It is naive but good to have on the table. There is a real question about long-term pharma commitment to something like this; they will play in the moment but will they play after the pandemic passes or the next generation of CEOs or R&D heads show up? To his credit, he points that out in slide 13.

Apart from the technology and monies needed, the political and ethical considerations are enormous. I don't see those in the equation. Paul Stoffels will see them. Getting funding via royalties is ok but availability, accessibility and affordability will be in the table.

Obviously, the idea is not new, we were doing this for TB, malaria and HIV drugs and vaccines years ago. What is new is the awakening that pharma, rather than Gates, can create a not-for-profit entity to do this and be an active contributor to it. The question is why use this construct? Why not just allow companies to form? To avoid competition in a field that few want to invest in or cover? The TB Alliance, MMV, IAVI, etc we're formed because pharma was not stepping up Maybe this NewCo can use pharma rather than Gates or government funding to sustain itself. I find it interesting that he proposes that these latter sectors should also contribute.

On the plus side, this might help to keep the momentum going. It is hugely important not to lose what we know and where we are scientifically today and build on that.

My bottom line: a good idea that needs more sophisticated thinking. M.

On Sep 2, 2020, at 7:06 AM, Collins, Francis (NIH/OD) [E] < (b) (6) wrote:

Hi all,

Please see the attached slide sets for this morning's Hever meeting on antivirals. We can discuss at the 8 AM War Room call.

I am pretty sure I will be asked whether ACTIV is willing to share materials that led to decisions about Go/Defer/No in Waves 1 – 3. Is there a file on each compound that was considered, and are we willing to provide that to interested parties?

Please check out the second attachment – does this compendium of antivirals contain any surprises?

Please look at Andy Plump's proposal about a NewCo for developing therapeutics in future pandemics. Does that make sense to you?

If I could get feedback (especially from Stacey and Joe) by 11 AM, that would be great!

Francis

From: (b) (6) (b) (6)
Sent: Tuesday, September 1, 2020 11:00 PM
Cc: (b) (6) (b) (6) Trevor Jones < (b) (6)
(b) (6) Geoff Frew < (b) (6) (b) (6) < (b) (6)
(b) (6) (b) (6) (b) (6) (b) (6) (b) (6)
(b) (6)
Subject: Hever COVID-19 Antivirals Meeting Sept 2 SLIDES AND MATERIAL

Dear All,

Please find enclosed

1) A master deck with presentation slides for tomorrow
2) An excel table with overview of compounds considered for the NIH ACTIV Antivirals Trial
3) COVID-19 antivirals small molecule overview slide deck

Please, note that Dr. Bradner's presentation Is not included in the circulated master deck as it was too big to send by e-mail. It alongside comprehensive background information will be circulated separately via a link..
For tomorrow we should be able however to run all slides from a single computer.

Looking forward to a good discussion.

Best Regards on behalf of Trevor and (b) (6)

(b) (6)

<HEVER September 2, 2020 COVID-19 Meeting Presentation vF SHORT.pdf>
<COVID 19 Antivirals Landscape_COVID19 R&D 2020-09.pdf>
<Table of Evaluated Antivirals for ACTIV 083120.pdf>

From: Adam, Stacey (FNIH) [T] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=DCD875F0679648859E1CF101C0943414-ADAMSJ4]
Sent: 8/31/2020 4:41:51 PM
To: Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]; Menetsk , Joseph (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5001af52dc4a427ea3d34f1e072f8cb7-menetskijp]
CC: George, Jill (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=f90bffb4b3a2464382adc29b127aed4e-georgejil]
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Thanks, Ashley!

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: (b) (6) · Mobile: (b) (6)

From: Parker, Ashley (NIH/OD) [E] < (b) (6)
Sent: Monday, August 31, 2020 12:38 PM
To: Menetski, Joseph (FNIH) [T] < (b) (6) Adam, Stacey (FNIH) [T] < (b) (6)
Cc: George, Jill (NIH/OD) [E] < (b) (6)
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Ok, thanks to you both. Attached is the clean version – Jill has done some minor editing and we've removed the FNIH logo since this is indicated on slide 2 and not needed on every slide.

Thanks and fingers crossed this is good enough!
Ashley

From: Menetski, Joseph (FNIH) [T] (b) (6)
Sent: Monday, August 31, 2020 12:35 PM
To: Parker, Ashley (NIH/OD) [E] < (b) (6) Adam, Stacey (FNIH) [T] <sad (b) (6)
Cc: George, Jill (NIH/OD) [E] < (b) (6)
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

If Stacey is OK, I am OK. This looks fine.

From: Parker, Ashley (NIH/OD) [E] < (b) (6)
Sent: Monday, August 31, 2020 11:43 AM
To: Adam, Stacey (FNIH) [T] (b) (6) >; Menetski, Joseph (FNIH) [T] < (b) (6)
Cc: George, Jill (NIH/OD) [E] (b) (6)
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Hi Stacey,

I greatly appreciate the notes and you identifying the issue with the table. Attached is a clean vers on of both the PP and table. Once you've cleared we will clean up and send to FC for final review and get this to Hever.

Thanks,

Ashley

From: Adam, Stacey (FNIH) [T] (b) (6)
Sent: Monday, August 31, 2020 10:15 AM
To: Parker, Ashley (NIH/OD) [E] < (b) (6) Menetski, Joseph (FNIH) [T] (b) (6)
Cc: George, Jill (NIH/OD) [E] (b) (6)
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Hi Ashley,

Thanks for putting this together. I have made notes in the attached pdf both on where the two agents I think are missing on the slides should go. Joe can confirm.
Also, for the pdf, the final column as some issues that I have also noted in the comments.

Thanks,
Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: (b) (6) | Mobile: (b) (6)

From: Parker, Ashley (NIH/OD) [E] (b) (6) >
Sent: Monday, August 31, 2020 9:55 AM
To: Menetski, Joseph (FNIH) [T] < (b) (6) Adam, Stacey (FNIH) [T] < (b) (6)
Cc: George, Jill (NIH/OD) [E] (b) (6)
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Thanks, Joe and Stacey. Attached is the revised slide set and we can share the attached summary Dolsten has requested w/ the host vs. directed as a separate attachment.

There are 2 agents on the list (table) that are not accounted for based on the complete list Joe provided (56 total) – I assume 2 compounds that should go in the NO GO section for wave 2. Can you please let me know where the discrepancy is here and I will add those to where they belong?

Once we have this – we can clean the slides up for visual edits.

Thanks,
Ashley

From: Menetski, Joseph (FNIH) [T] <j (b) (6)
Sent: Monday, August 31, 2020 9:21 AM
To: Adam, Stacey (FNIH) [T] (b) (6) ; Parker, Ashley (NIH/OD) [E] < (b) (6)
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

I think in most cases I left the Target as part of the MOA. Looking at the slides, I think that the MOA that was used was the short one, that was more general. As Stacey says below, if it is direct acting and inhibits a protease, it is the viral protease, etc.

Based on the MOA, you can see that the target is either host or one of the main viral proteins.

It would be fairly easy to go through and highlight Host versus direct (most are host). Maybe separate viral protease and polymerase. Maybe using color coding.

It would be helpful to know how the information is intended to be used or interpretation that Francis wants to make.

Joe

From: Adam, Stacey (FNIH) [T] (b) (6)
Sent: Monday, August 31, 2020 8:53 AM
To: Parker, Ashley (NIH/OD) [E] < (b) (6)
Cc: Menetski, Joseph (FNIH) [T] (b) (6)
Subject: RE: [EXTERNAL] RE: HEVER COVID 19 Antivirals meeting Sept 2 Slides

Hi Ashley,

Forgive me, but guess I am trying to understand what providing the specific target does on top of the fact that we have provided the MOA, and in Joe's spreadsheet that he sent last night he had coded the agents as either direct viral targeting or host targeting.

Joe, maybe this is my lack of knowledge in virology, but if we know it is a viral targeting agent and the MOA is that it inhibits a specific protease, is that not sufficient for the "target"? If so, then I think we have provided what Dolsten is asking for. If not then for some of the broad mechanistic actors, I am not sure we will have this information. Apologies, if I am missing some nuance.

Thanks,
Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct: (b) (6) Mobile: (b) (6)

From: Parker, Ashley (NIH/OD) [E] < (b) (6)
Sent: Monday, August 31, 2020 8:47 AM
To: Adam, Stacey (FNIH) [T] (b) (6)
Cc: Menetski, Joseph (FNIH) [T] (b) (6)
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Hi Stacey,

Should we propose including a chart of the antivirals with the targets, MOU, as a separate attachment? If so, could you provided this and I can let FC know that's the plan. I have no preference here but want to ensure we provide what Dolsten has requested.

I will share the revised sl des once we are done editing.

Thanks,
Ashley

From: Adam, Stacey (FNIH) [T] (b)
Sent: Monday, August 31, 2020 8:42 AM

To: Parker, Ashley (NIH/OD) [E] (b) (6)
Cc: Menetski, Joseph (FNIH) [T] (b) (6)
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Hi Ashley,

Given all of the information already on these slides and the worry that they are busy, do we really want to try to fit the category of host-targeted versus viral targeted on these slides?
Again, Joe and I can work through that this morning, but I am just curious how we propose to represent this, especially if you are going to list the specific targets themselves and not just perhaps color code them one versus the other.

Thanks,
Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct. (b) (6) Mobile: (b) (6)

From: Parker, Ashley (NIH/OD) [E] (b) (6)
Sent: Monday, August 31, 2020 8:39 AM
To: Adam, Stacey (FNIH) [T] (b) (6)
Cc: Menetski, Joseph (FNIH) [T] (b) (6)
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Hi Stacey,

I am modifying the slides but I still do not have the viral and host targets for these compounds. Can I send the excel spreadsheet for these to be added or do we not have those?

Thanks,
Ashley

From: Adam, Stacey (FNIH) [T] (b) (6)
Sent: Monday, August 31, 2020 8:36 AM
To: Parker, Ashley (NIH/OD) [E] < (b) (6)
Cc: Menetski, Joseph (FNIH) [T] (b) (6)
Subject: RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Hi Ashley,

I am now at my computer, sorry I was trekking to and from the gym this morning so was on my phone earlier.
Do you need some assistance modifying the slides still or is there anything you still need from Joe and I?

Thanks,
Stacey

Stacey J. Adam, PhD
Director, Cancer
Research Partnerships
Direct. (b) (6) Mobile: (b) (6)

From: Parker, Ashley (NIH/OD) [E] < (b) (6)
Sent: Monday, August 31, 2020 7:48 AM
To: Adam, Stacey (FNIH) [T] (b) (6)
Cc: Menetski, Joseph (FNIH) [T] (b) (6)
Subject: Re: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Sorry I forgot to mention there is no true back up slides — FC's slides will be merged with a larger presentation with other speakers.

Thanks,
Ashley

On Aug 31, 2020, at 7:44 AM, Parker, Ashley (NIH/OD) [E] (b) (6) wrote:

> Thanks, Stacey! We will now have 17 no go's for wave 2 or there are 2 other compounds to replace these if the total is in fact 19 for wave 2?
>
> Thanks,
> Ashley
>
> On Aug 31, 2020, at 7:35 AM, Adam, Stacey (FNIH) [T] < (b) (6) wrote:
>
> > Hi Ashley,
> >
> > The duplicates should remain in the "Defer" category.
> >
> > I would just split the no-go to a separate slide. Abs move it to back up.
> >
> > Joe, would you agree?
> >
> > Thanks,
> > Stacey
> >
> > Sent from my iPhone. Please excuse the brevity and typos.
> >
> > On Aug 31, 2020, at 7:13 AM, Parker, Ashley (NIH/OD) [E]
> > (b) (6) wrote:
> >
> > Yes, I agree and we can split slide 6 into two slides. I will standby for the other responses from Joe and Stacey before making the final edits.
> >
> > Thanks,
> > Ashley
> >
> > On Aug 31, 2020, at 5:13 AM, Collins, Francis (NIH/OD) [E]
> > < (b) (6) wrote:
> >
> > > Thanks for pulling this together at 3 AM (!),
> > > Ashley. I'll wait to see what Joe and Stacey want to

do about a final version. Slide 6 is going to be hard for people to read because of the large amount of information and the small font -- might this need to be broken into two slides?

FC

From: Parker, Ashley (NIH/OD) [E]
< (b) (6)
Sent: Monday, August 31, 2020 3 03 AM
To: Collins, Francis (NIH/OD) [E] (b) (6) ;
Wholley, David (FNIH) [T] (b) (6)
Menetski, Joseph (FNIH) [T] (b) (6)
Adam, Stacey (FNIH) [T] < (b) (6)
Cc: George, Jill (NIH/OD) [E] (b) (6) >
Subject: RE. [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Hi Francis et al.,

Attached is a revised version with the timelines of review for waves 1-3 prioritization efforts and the MOAs for most compounds. Joe – do we have information on viral and host targets? If so, please send and I can add this info to slides 5-7.

I found two duplications (b) (4) and (b) (4) listed in both deferred and NO-GO) on slide 6 and need clarification on these as well.

Otherwise does this set look closer to what you need for Hever? We will clean these up for visual purposes as well.

Thanks,
Ashley

From: Parker, Ashley (NIH/OD) [E]
Sent: Sunday, August 30, 2020 2:28 PM
To: Collins, Francis (NIH/OD) [E] (b) (6)
Wholley, David (FNIH) [T] (b) (6)
Menetski, Joseph (FNIH) [T] (b) (6)
Adam, Stacey (FNIH) [T] < (b) (6)
Subject: RE [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Hi Francis,

We will take care of it and send a version back to you for review.

Thanks,

Ashley

From: Collins, Francis (NIH/OD) [E]
(b) (6)
Sent: Sunday, August 30, 2020 2:26 PM
To: Parker, Ashley (NIH/OD) [E]
(b) (6) ; Wholley, David (FNIH) [T]
(b) (6) ; Menetski, Joseph (FNIH) [T]
(b) (6) , Adam, Stacey (FNIH) [T]
(b) (6)
Subject: FW: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Is it possible to group the antivirals from Waves 1 – 3 with these categories? Aren't they mostly "known viral targets"?

FC

From:(<
Sent: Sunday, August 30, 2020 10:56 AM
To: Collins, Francis (NIH/OD) [E] < (b) (6)
Cc: (b) (6) ;
Parker, Ashley (NIH/OD) [E] < (b) (6)
George, Jill (NIH/OD) [E] (b) (6) , Trevor Jones (b) (6) ;
(b) (6) ; Geoff Frew
<ge (b) (6)
Subject: Re: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Good suggestion

Maybe we can group drugs to be tested in order to make cross presenter summary

Known viral targets
Host targets
Unknown MOA

Or any other matrix you prefer

Sent from my iPhone

> On Aug 30, 2020, at 09:49, Collins, Francis (NIH/OD) [E]
> (b) (6) wrote:
>
> Hi (b) (6) ,

I'd be glad to provide a brief summary of the extensive prioritization process that ACTIV is following for antivirals. I could present this with a few slides in about five minutes. But this would fit much better as part of the session with Plump, Bradner, and Hudson, rather than inserted in the Discussion at the end. Might that rearrangement be possible?

Ashley can get slides to you by tomorrow.

Francis

From: (b) (6)

Sent: Sunday, August 30, 2020 9:16 AM
To: Collins, Francis (NIH/OD) [E]
(b) (6)
Cc: Parker, Ashley (NIH/OD) [E]
(b) (6) >; George, Jill (NIH/OD) [E] (b) (6)
(b) (6)
>; Trevor Jones
< (b) (6)
(b) (6) Geoff Frew
(b) (6) >;
(b) (6)

Subject: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Dear Francis

I hope this e-mail is reaching you well.

I understand from Trevor that he had agreed with you to do a quick update on antivirals ACTIV activities and plans as part of the discussion session in Wednesday session.

So just checking in if you would plan to have pre-read slides, and also if you plan to have presentation slides or run the discussion without slides?

I think planning for ~ 5 minutes so as part of the discussion probably will be appropriate. We only have 1 hour for this next meeting – so a bit shorter than previous meetings.

It would be great if you could let us know if you plan to have presentations slides so that we can integrate those.

Also if Ashley could help send pre-read slides to myself and Jill cc to Trevor ideally by Monday 5 pm EST.

Please, see current draft agenda below.

Looking forward to an exciting discussion.

Best wishes on behalf of (b) (6) and Trevor,
(b) (6)

<image001.jpg>

From: Adam, Stacey (FNIH) [T] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=DCD875F0679648859E1CF101C0943414-ADAMSJ4]
Sent: 8/31/2020 11:48:06 AM
To: Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]
CC: Menetski, Joseph (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5001af52dc4a427ea3d34f1e072f8cb7-menetskijp]
Subject: Re: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Hi Ashley,

No, no new compounds. Please just adjust the numbers.

Stacey

Sent from my iPhone. Please excuse the brevity and typos.

> On Aug 31, 2020, at 7:44 AM, Parker, Ashley (NIH/OD) [E] < (b) (6) wrote.
>
> Thanks, Stacey! We will now have 17 no go's for wave 2 or there are 2 other compounds to replace these if the total is in fact 19 for wave 2?
>
> Thanks,
> Ashley
>
> On Aug 31, 2020, at 7:35 AM, Adam, Stacey (FNIH) [T] < (b) (6) wrote:
>
> > Hi Ashley,
> >
> > The duplicates should remain in the "Defer" category.
> >
> > I would just split the no-go to a separate slide. Abs move it to back up.
> >
> > Joe, would you agree?
> >
> > Thanks,
> > Stacey
> >
> > Sent from my iPhone. Please excuse the brevity and typos.
> >
> > > On Aug 31, 2020, at 7:13 AM, Parker, Ashley (NIH/OD) [E]
> > > (b) (6) > wrote:
> > >
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Subject: Re: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Good suggestion

Maybe we can group drugs to be tested in order to make cross presenter summary

Known viral targets
Host targets
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Or any other matrix you prefer

Sent from my iPhone

On Aug 30, 2020, at 09:49, Collins, Francis (NIH/OD) [E] (b) (6) wrote:

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I'd be glad to provide a brief summary of the extensive prioritization process that ACTIV is following for antivirals. I could present this with a few slides in about five minutes. But this would fit much better as part of the session with Plump, Bradner, and Hudson, rather than inserted in the Discussion at the end. Might that rearrangement be possible?

Ashley can get slides to you by tomorrow.

Francis

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Also if Ashley could help send pre-read slides to myself and Jill cc to Trevor ideally by Monday 5 pm EST.

Please, see current draft agenda below.

Looking forward to an exciting discussion.

Best wishes on behalf of (b) (6) and Trevor,
(b) (6)

<image001.jpg>

From: Adam, Stacey (FNIH) [T] [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=DCD875F0679648859E1CF101C0943414-ADAMSJ4]
Sent: 8/31/2020 11:49:52 AM
To: Parker, Ashley (NIH/OD) [E] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=306b2244466140faa95aaaafe06ebd70-parkeras]
CC: Menetski, Joseph (FNIH) [T] [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=5001af52dc4a427ea3d34f1e072f8cb7-menetskijp]
Subject: Re: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides

Hi Ashley,

I think that is OK. You can just note that 17 were no-go on the slide.

Thanks, Stacey

Sent from my iPhone. Please excuse the brevity and typos.

> On Aug 31, 2020, at 7:48 AM, Parker, Ashley (NIH/OD) [E] < (b) (6) wrote:
>
> Sorry I forgot to mention there is no true back up slides — FC's slides will be merged with a larger presentation with other speakers.
>
> Thanks,
> Ashley
>
> On Aug 31, 2020, at 7:44 AM, Parker, Ashley (NIH/OD) [E] (b) (6) wrote:
>
> > Thanks, Stacey! We will now have 17 no go's for wave 2 or there are 2 other compounds to replace these if the total is in fact 19 for wave 2?
> >
> > Thanks,
> > Ashley
> >
> > On Aug 31, 2020, at 7:35 AM, Adam, Stacey (FNIH) [T] (b) (6) wrote:
> >
> > > Hi Ashley,
> > >
> > > The duplicates should remain in the "Defer" category.
> > >
> > > I would just split the no-go to a separate slide. Abs move it to back up.
> > >
> > > Joe, would you agree?
> > >
> > > Thanks,
> > > Stacey
> > >
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On Aug 31, 2020, at 7:13 AM, Parker, Ashley (NIH/OD) [E] (b) (6) wrote:

Yes, I agree and we can split slide 6 into two slides. I will standby for the other responses from Joe and Stacey before making the final edits.

Thanks,
Ashley

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> **Subject:** RE: [EXTERNAL] RE: HEVER COVID-19 Antivirals meeting Sept 2 - Slides
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I would agree. In fact, I would suggest making slide 6 look exactly same format as slide 5, just maybe put an asterisk next to the Merck/Ridgeback drug and a note that Merck elected to develop it on their own. Then move the existing slide 6 to backup. If Francis has 5 minutes, there is no way he's going to be able to go through the reasons each of the candidates in wave 2 were deferred or dropped anyway.

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